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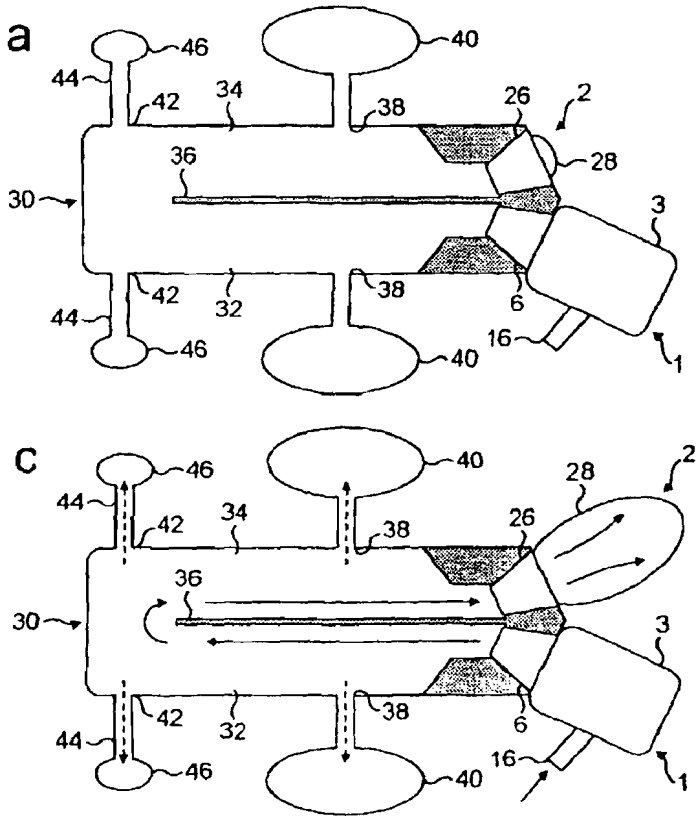

(57) Abstract: A nasal delivery device for and a method of delivering a substance to a nasal cavity of a subject, the delivery device comprising: a delivery unit for delivering a flow entraining a substance to one nostril of a subject, the delivery unit including a nosepiece for fitting to a nostril of the subject; and a flow resistor unit for fitting to the other nostril of the subject, the flow resistor unit including a progressive resistor for progressively providing an increasing flow resistance to the delivered flow.

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NASAL DEVICES

The present invention relates to a nasal delivery device for and a method of delivering a substance, in particular one of a liquid, as a suspension or solution, or a powder containing a medicament, especially systemic or topical pharmaceuticals, to the nasal airway of a subject.

There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitionin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa advantageously provides for rapid systemic uptake.

Nasal delivery is also expected to be advantageous for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and also other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

It is also expected that nasal delivery could provide an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

Furthermore, it is expected that nasal delivery using the nasal delivery technique of the present invention will prove effective in the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is

possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

Also, it is expected that the nasal delivery technique of the present invention will allow for the effective delivery of vaccines.

Aside from the delivery of medicaments, the irrigation of the nasal mucosa with liquids, in particular saline solutions, is commonly practised to remove particles and secretions, as well as to improve the mucociliary activity of the nasal mucosa. These solutions can be used in combination with active pharmaceuticals.

For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse effects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

WO-A-00/51672 discloses a delivery device for delivering a substance, in particular a medicament, in a bi-directional flow through the nasal cavities, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril. This bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

In one aspect the present invention provides a nasal delivery device for delivering a substance to a nasal cavity of a subject, comprising: a delivery unit for delivering a flow entraining a substance to one nostril of a subject, the delivery unit including a nosepiece for fitting to a nostril of the subject; and a flow resistor unit for fitting to the other nostril of the subject, the flow resistor unit including a progressive resistor for progressively providing an increasing flow resistance to the delivered flow.

In one embodiment the progressive resistor comprises an inflatable member which provides a progressively increasing resistance to the delivered flow.

In another embodiment the flow resistor unit includes a movable member which is movable under the action of a pressure developed in the nasal airway, and a biasing element for providing a progressively increasing resistance to the movement of the movable member.

Preferably, the flow resistor unit further includes a housing in which the movable member is movable, the housing including an aperture therein which is located such as to vent the housing when movable member is driven a predeterminable distance corresponding to a first predeterminable pressure, whereby the flow resistance decreases and the flow rate increases following the development of a second predeterminable pressure.

Preferably, the flow resistor unit includes a filter for collecting any vented material.

Preferably, the delivery unit includes a substance supply unit which is actuatable to supply a substance.

More preferably, the substance supply unit is actuatable by the progressive flow resistor unit.

In one embodiment the substance supply unit is configured to be actuated to supply a substance at a predeterminable pressure.

In another embodiment the substance supply unit is configured to be actuated to supply a substance at a predeterminable flow rate.

In a further embodiment the substance supply unit is configured to be actuated to supply a substance at one or both of a predeterminable pressure and a predeterminable flow rate.

Preferably, the delivery unit further includes a mouthpiece through which the subject in use exhales.

In one embodiment the delivery unit further includes a flow channel fluidly connecting the nosepiece and the mouthpiece, whereby exhaled air from an exhalation breath is delivered through the nosepiece.

In another embodiment the delivery unit further includes a flow channel fluidly connected to the nosepiece through which a gas flow, separate to an exhaled air flow from an exhalation breath of a subject, is in use delivered, and a gas supply unit for supplying a gas flow to the flow channel.

Preferably, the substance supply unit includes a dosing unit for supplying a substance.

In one embodiment the dosing unit comprises a nebulizer for supplying an aerosol.

In another embodiment the dosing unit comprises an aerosol canister for supplying an aerosol.

In a further embodiment the dosing unit comprises a delivery pump unit for supplying an aerosol.

In one preferred embodiment the dosing unit comprises a liquid pump unit for supplying a liquid aerosol.

In another preferred embodiment the dosing unit comprises a powder pump unit for supplying a powder aerosol.

In a yet further embodiment the dosing unit comprises a powder delivery unit for delivering a powder aerosol.

In another aspect the present invention provides a nasal delivery device for delivering a flow entraining a substance to a nostril of a subject, including: a nosepiece for fitting to a nostril of a subject; and a flow resistor upstream of the outlet of the nosepiece to provide a predeterminable flow resistance to the delivered flow.

In one embodiment the flow resistor is a progressive resistor for progressively providing an increasing flow resistance to the delivered flow.

In another embodiment the flow resistor is a fixed resistor for providing a predeterminable resistance to the delivered flow.

Preferably, the delivery device further includes: a substance supply unit which is actuatable to supply a substance.

In one embodiment the substance supply unit is configured to be actuated to supply a substance at a predeterminable pressure.

In another embodiment the substance supply unit is configured to be actuated to supply a substance at a predeterminable flow rate.

In a further embodiment the substance supply unit is configured to be actuated to supply a substance at one or both of a predeterminable pressure and a predeterminable flow rate.

Preferably, the delivery device further includes: a mouthpiece through which the subject in use exhales.

In one embodiment the delivery device further includes: a flow channel fluidly connecting the nosepiece and the mouthpiece, whereby exhaled air from an exhalation breath is delivered through the nosepiece.

In another embodiment the delivery device further includes: a flow channel fluidly connected to the nosepiece through which a gas flow, separate to an exhaled air flow from an exhalation breath of a subject, is in use delivered; and a gas supply unit for supplying a gas flow to the flow channel.

Preferably, the substance supply unit includes a dosing unit for supplying a substance.

In one embodiment the dosing unit comprises a nebulizer for supplying an aerosol.

In another embodiment the dosing unit comprises an aerosol canister for supplying an aerosol.

In a further embodiment the dosing unit comprises a delivery pump unit for supplying an aerosol.

In one preferred embodiment the dosing unit comprises a liquid pump unit for supplying a liquid aerosol.

In another preferred embodiment the dosing unit comprises a powder pump unit for supplying a powder aerosol.

In a yet further embodiment the dosing unit comprises a powder delivery unit for delivering a powder aerosol.

In a further aspect the present invention provides a method of delivering a substance to a nasal cavity of a subject, comprising the steps of: delivering a flow entraining a substance to one nostril of a subject; and progressively providing an increasing flow resistance to the delivered flow.

Preferably, the method further comprises the step of: decreasing the flow resistance on development of a predeterminable pressure.

In a yet further aspect the present invention provides a method of delivering a flow entraining a substance to a nostril of a subject, comprising the steps of: delivering a flow entraining a substance to a nostril of a subject; and providing a predeterminable flow resistance to the delivered flow.

In one embodiment the step of providing a predeterminable flow resistance to the delivered flow comprises the step of: progressively providing an increasing flow resistance to the delivered flow.

In another embodiment the step of providing a predeterminable flow resistance to the delivered flow comprises the step of: providing a predeterminable resistance to the delivered flow.

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figure 1(a) schematically illustrates the delivery unit of a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 1(b) illustrates the nasal delivery device of Figure 1(a) in the actuated configuration;

Figure 2(a) illustrates the flow resistor unit of the nasal delivery device of the first embodiment of the present invention;

Figure 2(b) illustrates the flow resistor unit of Figure 2(a) in which the flow resistor thereof is partially inflated at a pressure corresponding to the actuation pressure of the delivery unit;

Figure 2(c) illustrates the flow resistor unit of Figure 2(a) in which the flow resistor thereof is inflated at an increased pressure greater than the actuation pressure of the delivery unit;

Figure 3(a) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the first embodiment of the present invention fitted to the respective nostrils of a subject, where the subject is not exhaling through the mouthpiece of the delivery unit;

Figure 3(b) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the first embodiment of the present invention fitted to the respective nostrils of a subject, where the subject has commenced exhaling through the mouthpiece of the delivery unit and the pressure developed in the nasal airway is at the actuation pressure of the delivery unit;

Figure 3(c) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the first embodiment of the present invention fitted to the respective nostrils of a subject, where the delivery unit has been actuated and the subject is continuing to exhale through the mouthpiece of the delivery unit such as to develop an increased pressure in the nasal airway;

Figure 4(a) illustrates the flow resistor unit of a nasal delivery device in accordance with a second embodiment of the present invention;

Figure 4(b) illustrates the flow resistor unit of Figure 4(a) in which the progressive flow resistor thereof is partially driven at a pressure corresponding to the actuation pressure of the delivery unit;

Figure 4(c) illustrates the flow resistor unit of Figure 4(a) in which the progressive flow resistor thereof is driven at an increased pressure greater than the actuation pressure of the delivery unit;

Figure 5(a) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the second embodiment of the present invention fitted to the respective nostrils of a subject, where the subject is not exhaling through the mouthpiece of the delivery unit;

Figure 5(b) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the second embodiment of the present invention fitted to the respective nostrils of a subject, where the subject has

commenced exhaling through the mouthpiece of the delivery unit and the pressure developed in the nasal airway is at the actuation pressure of the delivery unit;

Figure 5(c) illustrates the delivery unit and the flow resistor unit of the nasal delivery device of the second embodiment of the present invention fitted to the respective nostrils of a subject, where the delivery unit has been actuated and the subject is continuing to exhale through the mouthpiece of the delivery unit such as to develop an increased pressure in the nasal airway;

Figure 6(a) schematically illustrates the delivery unit of a nasal delivery device in accordance with a third embodiment of the present invention;

Figure 6(b) illustrates the nasal delivery device of Figure 6(a) in the actuated configuration;

Figure 7(a) schematically illustrates the delivery unit of a nasal delivery device in accordance with a fourth embodiment of the present invention;

Figure 7(b) illustrates the nasal delivery device of Figure 7(a) in the actuated configuration;

Figure 8(a) illustrates the nasal delivery device of the fourth embodiment of the present invention fitted to a nostril of a subject, where the subject is not exhaling through the mouthpiece of the delivery unit;

Figure 8(b) illustrates the nasal delivery device of the fourth embodiment of the present invention fitted to a nostrils of a subject, where the delivery device has been actuated and the subject is continuing to exhale through the mouthpiece of the delivery device;

Figure 9(a) schematically illustrates a nasal delivery device in accordance with a fifth embodiment of the present invention;

Figure 9(b) illustrates the nasal delivery device of Figure 9(a) in the actuated configuration;

Figure 10(a) schematically illustrates a nasal delivery device in accordance with a sixth embodiment of the present invention;

Figure 10(b) illustrates the nasal delivery device of Figure 10(a) in the actuated configuration;

Figure 11(a) schematically illustrates a nasal delivery device in accordance with a seventh embodiment of the present invention;

Figure 11(b) schematically illustrates the nasal delivery device of Figure 11(a) in a primed, but inoperative configuration;

Figure 11(c) schematically illustrates the nasal delivery device of Figure 11(a) in an operative configuration;

Figure 11(d) schematically illustrates the nasal delivery device of Figure 11(a) in an actuated configuration;

Figure 12(a) illustrates the nasal delivery device of the seventh embodiment of the present invention fitted to a nostril of a subject, where the subject is not exhaling through the mouthpiece of the delivery unit; and

Figure 12(b) illustrates the nasal delivery device of the seventh embodiment of the present invention fitted to a nostril of a subject, where the delivery device has been actuated and the subject is continuing to exhale through the mouthpiece of the delivery device.

Figures 1 and 2 illustrate respectively a delivery unit 1 and a flow resistor unit 2 of a nasal delivery device in accordance with a first embodiment of the present invention.

The delivery unit 1 comprises a housing 3 which includes a tubular member 4, in this embodiment a cylindrical member, and a nosepiece 6 for fitting in one nostril of a subject which is disposed to one, the distal, end of the tubular member 4.

The tubular member 4 includes a cavity 8 at the one end thereof which is in fluid communication with the nosepiece 6 such that exhalation breath introduced thereinto is directed through the nosepiece 6.

The delivery unit 1 further comprises a substance supply unit 12 for delivering metered doses of a substance, in this embodiment an aerosol canister for delivering metered volumes of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing medicament, either as a suspension or solution. In this embodiment the substance supply unit 12 is configured to deliver substance which comprises a relatively large fraction of small particles.

The substance supply unit 12 is primeable, in this embodiment by loading a biasing element, and includes a release mechanism which, when triggered, releases the biasing element and actuates the substance supply unit 12 to deliver a metered dose of a substance.

In an alternative embodiment the substance supply unit 12 could comprise a mechanical delivery pump, in particular a liquid delivery pump or a powder delivery pump, which delivers metered doses of a substance on actuation thereof.

In another alternative embodiment the substance supply unit 12 could comprise a dry powder delivery unit which delivers metered doses of a substance, as a dry powder, on actuation thereof.

In yet another alternative embodiment the substance supply unit 12 could comprise a nebulizer which delivers metered doses of a substance, as an aerosol spray, on actuation thereof.

The delivery unit 1 further comprises a nozzle 14 which is fluidly connected to the substance supply unit 12 for providing an aerosol spray through the nosepiece 6. In this embodiment the nozzle 14 is disposed in the nosepiece 6 co-axially with the same.

The housing 3 further includes a mouthpiece 16 which is in fluid communication with the chamber 8 in the tubular member 4 and through which a subject exhales to actuate the substance supply unit 12, as will be described in more detail hereinbelow.

The delivery unit 1 further comprises a trigger mechanism 18 which is configured as to be actuatable to cause actuation of the substance supply unit 12 on the generation of a predetermined actuation pressure within the chamber 8 in the tubular member 4.

The trigger mechanism 18 includes a flexible member 20, in this embodiment a resilient membrane, which defines a part of the wall of the chamber 8 in the tubular member 4, and a link 22 which couples the flexible member 20 and the release mechanism of the substance supply unit 12. The flexible member 40 is

configured such as, on generation of a predetermined actuation pressure within the chamber 8 in the tubular member 4, to be deflected sufficiently as to actuate the release mechanism of the substance supply unit 12 and deliver a metered dose of a substance (as illustrated in Figure 1(b)).

The flow resistor unit 2 comprises a nosepiece 26 for fitting in the other nostril of the subject and a progressive flow resistor 28 in fluid communication therewith.

The progressive flow resistor 28, in this embodiment a balloon, provides a progressively increasing resistance to the exhaled air from the exhalation breath of a subject. Figures 2(a) to (c) illustrate respectively the progressive flow resistor 28 when not inflated, inflated at the actuation pressure of the delivery unit 1, and inflated at a pressure in excess of the actuation pressure of the delivery unit 1. In this embodiment the progressive flow resistor 28 also acts as an indicator for providing an indication as to operation of the delivery device.

Operation of the delivery device will now be described hereinbelow with reference to Figures 3(a) to (c), which drawings diagrammatically illustrate the nasal airway 30 of a human subject. The nasal airway 30 comprises the two nasal cavities 32, 34 separated by the nasal septum 36, which airway 30 includes numerous ostia, such as the paranasal sinus ostia 38 connected to the paranasal sinuses 40 and the tubal ostia 42 connected to the tuba auditiva 44 and the middle ears 46, and olfactory cells, and is lined by the nasal mucosa.

Firstly, the delivery unit 1 is inserted in one nostril of a subject and the flow resistor unit 2 is inserted in the other nostril of the subject.

The subject then begins to exhale through the mouthpiece 16 of the delivery unit 1, which exhalation acts to close the oropharyngeal velum of the subject and increase the pressure in the nasal airway 30 by the introduction of exhaled air from the exhalation breath thereinto, with the progressive flow resistor 28 providing an increased resistance to the exhaled air flow. The pressure in the nasal airway 30 increases rapidly until the actuation pressure of the delivery unit 1 is reached, at which point the substance supply unit 12 of the delivery unit 1 is actuated to deliver a metered dose of a substance to the nasal airway 30. The actuation pressure of the delivery unit 1 is less than that normally required to open the ostia in the nasal airway 30, notably the paranasal sinus ostia 38 and the tubal ostia 42. In this embodiment the delivery rate from the substance supply unit 12 is low such that the airborne particles are resident in the nasal airway 30 for a long period of time.

The subject continues to exhale through the mouthpiece 16 of the delivery unit 1, with the progressive flow resistor 28 providing an increasing resistance to the exhaled air flow, in this embodiment by inflation of the balloon. The pressure in the nasal airway 30 increases until the opening pressure for the paranasal sinus ostia 38 and the tubal ostia 42 is reached, at which point substance is driven into the paranasal sinuses 40 and the tuba auditiva 44 and the middle ears 46. In this embodiment the nasal airway 30 acts as a spacer for containing small airborne particles having an optimal particle size, typically in the range of from about 1 μm to about 10 μm for penetration into the paranasal sinuses 40 and the tuba auditiva 44 and the middle ears 46.

By using a progressive exit resistor, the pressure will gradually build up until the opening pressure is reached. This pressure is typically from about 0 to about 140 cmH_2O (≈0-1.4 kPa) in normal subjects. In one study of subjects with impaired tubal function and middle ear pathology, half had an opening pressure in this range, while the remaining subjects needed a higher pressure or could not open the tuba auditiva. In another study, a pressure of form about 100 to about 200 cmH_2O (≈ 1 to 2 kPa) was required to flush air through the tuba auditiva.

In this embodiment the speed of the delivered aerosol is slowed significantly as compared, for example, to conventional pMDIs, allowing for a greater uptake of substance. A significant problem with conventional pMDIs is the high release speed of the aerosol. This high speed is disadvantageous not only for inhalation to the lungs, but also nasal delivery. The reason is that the aerosol particles are shot against the nasal mucosa which leads to increased deposition in the mouth and the anterior regions of the nasal cavities. A soft mist inhaler using mechanical energy to produce small particles reduces the speed of the delivered particles by a factor of five.

In this embodiment the optimal mean particle size is between about 10 μm and about 30 μm. pMDIs generally produce smaller particles, but the particle size can be increased by one or both of reducing the driving pressure in the pMDI and modifying the dimensions of the nozzle 14. Traditional spray pumps normally produce particles with a mean particle size of from about 50 μm to about 60 μm, but simple modification allows mean particle sizes of from about 25 μm to about 30 μm to be generated. Specialized mechanical pumps can generate aerosol mists with mean particle sizes down to 5 μm (NebuHaler, Boehringer Ingelheim). A nebulizer is also available (PARI) for the generation of aerosol mists which have a mean particle size of about 10 μm.

Figure 4 illustrates the flow resistor unit 2 of a delivery device in accordance with a second embodiment of the present invention. The delivery unit 1 is of the same construction as the delivery unit 1 of the delivery device of the above-described first embodiment.

The flow resistor unit 2 comprises a nosepiece 26 for fitting in the other nostril of the subject and a progressive flow resistor 28 in fluid communication therewith.

The progressive flow resistor 28 provides a progressively increasing resistance to the exhaled air from the exhalation breath of a subject. Figures 4(a) to (c) illustrate respectively the progressive flow resistor 28 where the subject is not exhaling, the pressure in the nasal airway 30 is at the actuation pressure of the delivery unit 1, and the pressure in the nasal airway is at a pressure in excess of the actuation pressure of the delivery unit 1. In this embodiment the progressive flow resistor 28 also acts as an indicator for providing an indication as to the operation of the delivery device.

The progressive flow resistor 28 comprises a housing 47 which defines a chamber 48 which is in fluid communication with the nosepiece 26, a piston member 50 which is slideable in the chamber 48 under the action of the pressure developed in the nasal airway 30, and a biasing element 52, in this embodiment a resilient element, in particular a compression spring, for providing a progressively increasing resistance to the movement of the piston member 50.

In this embodiment the housing 47 includes an aperture 54 therein which is located such as to provide a vent to the atmosphere when the piston member 50 is driven a predetermined distance through the chamber 48 which corresponds to a pressure which exceeds the opening pressure for the paranasal sinus ostia 38 and the tubal ostia 42. With this configuration, the flow resistance gradually decreases and the air flow increases following the development of a pressure exceeding the opening pressure for the paranasal sinus ostia 38 and the tubal ostia 42. This pressure and flow regime promotes the deposition of airborne particles in the nasal airway 30. Furthermore, this pressure and flow regime ensures that airborne particles are flushed out of the nasal airway before the procedure is terminated, thereby preventing airborne particles, which could subsequently be inhaled, from remaining in the nasal airway 30.

In a preferred embodiment the progressive flow resistor 28 can comprise a filter for collecting any vented substance.

Operation of the delivery device will now be described hereinbelow with reference to Figures 5(a) to (c). Operation of the delivery device is the same as for the above-described first embodiment, with the biasing element 52 providing a progressively increasing resistance to the movement of piston member 50, and the aperture 54 in the housing 47 venting exhaled air from the exhalation breath of a subject to the atmosphere when the piston member 50 is driven a predetermined distance through the chamber 48 which corresponds to a pressure which exceeds the opening pressure for the paranasal sinus ostia 38 and the tubal ostia 4, whereby the flow resistance in the nasal airway 30 gradually decreases and the air flow increases following the development of a pressure exceeding the opening pressure for the paranasal sinus ostia 38 and the tubal ostia 42.

Figure 6 illustrates the delivery unit 1 of a delivery device in accordance with a third embodiment of the present invention. The flow resistor unit 2 is of the same construction as the flow resistor unit 2 of the delivery device of the above-described first embodiment.

The delivery unit 1 of this embodiment is very similar to the delivery unit 1 of the above-described first embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts

The delivery unit 1 of this embodiment differs from that of the above-described first embodiment in further comprising an exhalation breath actuatable gas delivery unit 58 for delivering a gas flow to the chamber 8 in the housing 4 in response to exhalation by a subject, and in that the mouthpiece 16 is in fluid communication with the gas delivery unit 58 and not the chamber 8 in the housing 4, whereby a gas flow is delivered to the chamber 8 in the housing 4, and hence the nasal airway 30, in response to exhalation through the mouthpiece 16.

Operation of the delivery device is the same as for the above-described first embodiment, with a gas flow being delivered to the chamber 8 in the housing 4, and hence a pressure being developed in the nasal airway 30, in response to exhalation through the mouthpiece 16.

Figures 7(a) and (b) illustrate a nasal delivery device in accordance with a fourth embodiment of the present invention.

The delivery device comprises a housing 103 which includes a tubular member 104, in this embodiment a cylindrical member, and a nosepiece 106 for fitting in one nostril of a subject which is disposed to one, the distal, end of the tubular member 104.

The tubular member 104 includes a chamber 108 at the one end thereof which is in fluid communication with the nosepiece 106 such that exhalation breath introduced thereinto is directed through the nosepiece 106.

The chamber 108 includes a flow resistor 109 which acts to restrict flow and thereby provide a flow resistance to an air flow driven through the chamber 198. In this embodiment the flow resistor 109 comprises a baffle which has a fixed flow resistance. With this configuration, the flow resistor 109 can be configured to provide the flow-limiting resistance, where this resistance is greater than the total nasal resistance, in the flow path through the delivery device and the nasal airway of the subject, and thereby provide for a maximum predetermined flow rate at the actuation pressure of the delivery device.

The delivery device further comprises a substance supply unit 112 for delivering metered doses of a substance, in this embodiment an aerosol canister for delivering metered volumes of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing medicament, either as a suspension or solution. In this embodiment the substance supply unit 112 is configured to deliver substance which comprises a relatively large fraction of small particles.

The substance supply unit 112 is primeable, in this embodiment by loading a biasing element, and includes a release mechanism which, when triggered, releases the biasing element and actuates the substance supply unit 112 to deliver a metered dose of a substance.

In an alternative embodiment the substance supply unit 112 could comprise a mechanical delivery pump unit, in particular a liquid delivery unit or a powder delivery unit, which delivers metered doses of a substance on actuation thereof.

In another alternative embodiment the substance supply unit 112 could comprise a dry powder delivery unit which delivers metered doses of a substance, as a dry powder, on actuation thereof.

In yet another alternative embodiment the substance supply unit 112 could comprise a nebulizer which delivers metered doses of a substance, as an aerosol spray, on actuation thereof.

The delivery device further comprises a nozzle 114 which is fluidly connected to the substance supply unit 112 for providing an aerosol spray through the nosepiece 106. In this embodiment the nozzle 114 is disposed in the nosepiece 106 co-axially with the same.

The housing 103 further includes a mouthpiece 116 which is in fluid communication with the chamber 108 in the tubular member 104 and through which a subject exhales to actuate the substance supply unit 112, as will be described in more detail hereinbelow.

The delivery device further comprises a trigger mechanism 118 which is configured as to be actuatable to cause actuation of the substance supply unit 112 on the generation of a predetermined actuation pressure within the chamber 108 in the tubular member 104, and hence the nasal airway of the subject.

The trigger mechanism 118 includes a flexible member 120, in this embodiment a resilient membrane, which defines a part of the wall of the chamber 108 in the tubular member 104, and a link 122 which couples the flexible member 120 and the release mechanism of the substance supply unit 112. The flexible member 120 is configured such as, on generation of a predetermined actuation pressure within the chamber 108 in the tubular member 104, to be deflected sufficiently as to actuate the release mechanism of the substance supply unit 112 and deliver a metered dose of a substance (as illustrated in Figure 7(b)).

Operation of the delivery device will now be described hereinbelow with reference to Figures 8(a) and (b), which drawings diagrammatically illustrate the nasal airway 130 of a human subject. The nasal airway 130 comprises the two nasal cavities 132, 134 separated by the nasal septum 136, which airway 130 includes numerous ostia, such as the paranasal sinus ostia 138 connected to the paranasal sinuses 140 and the tubal ostia 142 connected to the tuba auditiva 144 and the middle ears 146, and olfactory cells, and is lined by the nasal mucosa.

Firstly, the nosepiece 106 of the delivery device is inserted in one nostril of a subject. The subject then begins to exhale through the mouthpiece 16, which exhalation acts to close the oropharyngeal velum of the

subject and increase the pressure in the nasal airway 130 by the introduction of exhaled air from the exhalation breath thereinto, with the flow resistor 109 providing a fixed resistance to the exhaled air flow, and thereby providing for a predetermined flow rate from the delivery device. The pressure in the nasal airway 130 increases rapidly until the actuation pressure of the delivery device is reached, at which point the substance supply unit 112 is actuated to deliver a metered dose of a substance to the nasal airway 130. By the provision of the flow resistor 109 which has a flow resistance R_{FR} greater than the combined flow resistances of the inlet and outlet flow resistances R_I, R_O, the flow rate through the nasal airway 130 is advantageously at a predetermined flow rate on actuation of the delivery device, thereby providing for a predetermined residence time of substance in the nasal airway 130.

Figures 9(a) and (b) illustrate a delivery device in accordance with a fifth embodiment of the present invention.

The delivery device of this embodiment is very similar to the delivery device of the above-described fourth embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts

The delivery device of this embodiment differs from that of the above-described fourth embodiment in further comprising an exhalation breath actuatable gas delivery unit 158 for delivering a gas flow to the chamber 108 in the housing 104 in response to exhalation by a subject, and in that the mouthpiece 116 is in fluid communication with the gas delivery unit 158 and not the chamber 108 in the housing 104, whereby a gas flow is delivered to the chamber 108 in the housing 104, and hence the nasal airway 130, in response to exhalation through the mouthpiece 116.

Operation of the delivery device is the same as for the above-described fourth embodiment, with a gas flow being delivered to the chamber 108 in the housing 104, and hence a pressure being developed in the nasal airway 130, in response to exhalation through the mouthpiece 116.

Figures 10(a) and (b) illustrate a delivery device in accordance with a sixth embodiment of the present invention.

The delivery device of this embodiment is very similar to the delivery device of the above-described fourth embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts

The delivery device of this embodiment differs from that of the above-described fourth embodiment in not including a trigger mechanism 118, the substance supply unit 112 instead being actuated by a subject, and in that the nosepiece 106 defines a substance-receiving chamber 160 for receiving an aerosol cloud of substance delivered from the substance supply unit 112 through the nozzle 114. With this configuration, the chamber 160 in the nosepiece 106 functions as a spacer.

Operation of the delivery device is the same as for the above-described fourth embodiment, with the exception that the substance supply unit 112 is actuated manually and, subsequent to actuation, the subject exhales through the mouthpiece 116 to drive an air flow having a predetermined air flow rate, which is determined by the flow resistor 109, through the nosepiece 106 such as to entrain delivered substance and transfer the same into the nasal airway 130.

Figures 11(a) to (e) illustrate a nasal delivery device in accordance with a seventh embodiment of the present invention.

The delivery device comprises a housing 232 which includes an air chamber 234 for receiving the exhalation breath of a subject, a nosepiece 240 for fitting in a nostril of a subject which is in fluid communication with the air chamber 234 in the housing 232 and disposed to one, the distal, end of the housing 232, and a mouthpiece 241 through which the subject exhales and which is in fluid communication with the air chamber 234 in the housing 232.

The nosepiece 240 includes a channel 242 through which an air flow is delivered to the nasal airway of a subject.

The delivery device further comprises a channel blocking unit 243 for progressively blocking the channel 242 in the nosepiece 240 in response to an increasing pressure in the air chamber 234 in the housing 232, thereby providing a progressively increasing resistance to an air flow being driven therethrough.

In this embodiment the channel blocking unit 243 comprises a diaphragm 244, in this embodiment a resilient member, which defines a part of the wall of the air chamber 234 in the housing 232, and first and second blocking elements 245, 246, in this embodiment flexible sheet elements, which are guided by respective ones of first and second guides 247, 248 and coupled to respective ones of the blocking elements 245, 246 such as to extend into the channel 242 in the nosepiece 240 on deflection of the diaphragm 244. The diaphragm 244 is configured such as to be progressively deflected with an increasing pressure in the air chamber 234 in the housing 232, such that the blocking elements 245, 246 coupled thereto are progressively extended into the channel 242 in the nosepiece 240 with an increasing pressure in the air chamber 234 in the housing 232, and block the channel 242 in the nosepiece 240 to a predetermined extent on the generation of a pressure in the air chamber 234 in the housing 232 corresponding to the actuation pressure of the substance supply unit 264.

The delivery device further comprises a nozzle 256 for providing an aerosol spray through the nosepiece 240. The nozzle 256 comprises a head 258 which is located, in this embodiment co-axially, within the nosepiece 240, and a delivery tube 262 which is fluidly connected to the head 258.

The delivery device further comprises a substance supply unit 264 for delivering a metered dose of a substance, in this embodiment a metered volume of a liquid containing medicament, either as a suspension or solution, to the nozzle 256.

In this embodiment the substance supply unit 264 comprises a mechanical delivery pump 266, in particular a spray pump, which is coupled to the nozzle 256 and is configured, on actuation, to deliver a metered dose of a substance, in this embodiment a liquid containing medicament, either as a suspension or solution, as an aerosol spray. The delivery pump 266 is movable relative to the nozzle 256 from a first, non-actuated position (as illustrated in Figures 11(a) to (c)) to a second, actuated position (as illustrated in Figure 11(d)) in which a metered dose of substance has been delivered.

In an alternative embodiment the substance supply unit 264 could comprise an aerosol canister for delivering metered volumes of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing medicament.

The substance supply unit 264 further comprises a biasing element 268, in this embodiment a resilient element, particularly a compression spring, for biasing the delivery pump 266 in an actuating direction when in the non-actuated position, and a loading member 270, in this embodiment first and second levers, for loading the biasing element 268 such as to bias the delivery pump 266, when in the non-actuated position,

with an actuation force. The loading member 270 is movable between a first, rest position in which the biasing element 268 is not loaded thereby, and a second, operative position in which the biasing element 268, when restrained by the delivery pump 266, loads the delivery pump 266 with the actuation force.

The delivery device further comprises a trigger mechanism 274 which is configured to be actuatable to cause the actuation of the substance supply unit 264. In this embodiment the trigger mechanism 274 is configured to be actuatable to cause actuation of the substance supply unit 264 on generation of a predetermined pressure in the air chamber 234 in the housing 232.

The trigger mechanism 274 comprises first and second stop members 276, 278, and first and second biasing elements 280, 282, in this embodiment resilient elements, particularly compression springs, which act to bias respective ones of the first and second stop members 276, 278 inwardly to a stop position (as illustrated in Figures 11(a) to (c)) in which the first and second stop members 276, 278 act to prevent movement of the delivery pump 266 from the non-actuated position to the actuated position.

The trigger mechanism 274 further comprises first and second arms 286, 288 which are pivotable about respective pivots 290, 292 and coupled at one end thereof to respective ones of the first and second stop members 276, 278 such that pivoting of the arms 286, 288 to a release position causes the respective ones of the stop members 276, 278 to which the arms 286, 288 are coupled to be moved outwardly against the bias of the first and second biasing elements 280, 282 to a release position (as illustrated in Figure 11(d)) in which the stop members 276, 278 are disposed outwardly of the head of the delivery pump 266, such that the delivery pump 266, when biased by the biasing element 268, is driven to the actuated position. In being driven to the actuated position, a metered dose of a substance is delivered from the nozzle 256 as an aerosol spray.

The trigger mechanism 274 further comprises a diaphragm 296, in this embodiment a resilient member, which defines a part of the wall of the air chamber 234 in the housing 232. The diaphragm 296 is configured such as, on generation of a predetermined actuation pressure within the air chamber 234 in the housing 232, to be deflected such as to engage the other, distal ends of the arms 286, 288 and cause the same to be pivoted to the release position. At this actuation pressure, the blocking elements 245, 246 of the channel blocking unit 243 block the channel 242 in the nosepiece 240 to a predetermined extent such that the flow rate of an air flow driven therethrough is at a predetermined value on actuation.

With this configuration, the flow rate of exhaled air from an exhalation breath of a user decreases progressively as the pressure in the air chamber 234 in the housing 232 increases to a predetermined flow rate at a pressure corresponding to the actuation pressure of the substance supply unit 264.

Operation of the delivery device will now be described hereinbelow with reference to Figures 12(a) and (b), which drawings diagrammatically illustrate the nasal airway 330 of a human subject. The nasal airway 330 comprises the two nasal cavities 332, 334 separated by the nasal septum 336, which airway 330 includes numerous ostia, such as the paranasal sinus ostia 338 connected to the paranasal sinuses 340 and the tubal ostia 342 connected to the tuba auditiva 344 and the middle ears 346, and olfactory cells, and is lined by the nasal mucosa.

Firstly, the substance supply unit 264 is primed by operating the loading members 270 to load the biasing element 268. The nosepiece 240 of the delivery device is then inserted in one nostril of a subject. The subject then begins to exhale through the mouthpiece 241, which exhalation acts to close the oropharyngeal velum of the subject and increase the pressure in the air chamber 234 in the housing 232, and hence the nasal airway 330, by the introduction of exhaled air from the exhalation breath thereinto. With this

increasing pressure in the air chamber 234 in the housing 232, the diaphragm 244 of the channel blocking unit 243 is progressively deflected and the blocking elements 245, 246 of the channel locking unit 243 coupled thereto are progressively extended into the channel 242 in the nosepiece 240. Also with this increasing pressure in the air chamber 234 in the housing 232, the diaphragm 296 of the trigger mechanism 274 is progressively deflected. When the pressure in the air chamber 234 in the housing 232 reaches the actuation pressure of the substance supply unit 264, the diaphragm 296 of the trigger mechanism 274 is deflected such as to engage the other, distal ends of the arms 286, 288 of the trigger mechanism and cause the same to be pivoted to the release position, whereby the trigger mechanism 274 is actuated and enables actuation of the substance supply unit 264. At this actuation pressure, the blocking elements 245, 246 of the channel blocking unit 243 block the channel 242 in the nosepiece 240 to a predetermined extent such that the flow rate of an air flow driven therethrough is at a predetermined value on actuation.

A yet further advantage is that the air flow acts to create a positive pressure inside the nasal cavities connected in series, which tends to expand and widen narrow and congested regions.

A further advantage is that the nosepiece 6 of the delivery unit 1 acts to expand the narrowest, anterior part of the nasal cavity 32 to which substance is delivered, and thereby reduces the unwanted high deposition in the anterior region of the nasal cavity 32 which is lined by squamous epithelium.

Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined by the appended claims.

For example, in one modification, the flow resistor unit 2 of the above-described first and second embodiments could comprise an electrically-operable progressive resistor 28 such as to provide for a flow resistance having a predeterminable profile.

In addition, in another modification, and particularly through the use of an electrically-operable progressive resistor 28, the substance supply unit 12 could be operable in response to an input from the flow resistor unit 2.

CLAIMS

1. A nasal delivery device for delivering a substance to a nasal cavity of a subject, comprising:
a delivery unit for delivering a flow entraining a substance to one nostril of a subject, the delivery unit including a nosepiece for fitting to a nostril of the subject; and
a flow resistor unit for fitting to the other nostril of the subject, the flow resistor unit including a progressive resistor for progressively providing an increasing flow resistance to the delivered flow.

2. The delivery device of claim 1, wherein the progressive resistor comprises an inflatable member which provides a progressively increasing resistance to the delivered flow.

3. The delivery device of claim 1, wherein the flow resistor unit includes a movable member which is movable under the action of a pressure developed in the nasal airway, and a biasing element for providing a progressively increasing resistance to the movement of the movable member.

4. The delivery device of claim 3, wherein the flow resistor unit further includes a housing in which the movable member is movable, the housing including an aperture therein which is located such as to vent the housing when movable member is driven a predeterminable distance corresponding to a first predeterminable pressure, whereby the flow resistance decreases and the flow rate increases following the development of a second predeterminable pressure.

5. The delivery device of claim 4, wherein the flow resistor unit includes a filter for collecting any vented material.

6. The delivery device of any of claims 1 to 5, wherein the delivery unit includes a substance supply unit which is actuatable to supply a substance.

7. The delivery device of claim 6, wherein the substance supply unit is configured to be actuatable by the progressive flow resistor unit.

8. The delivery device of claim 6 or 7, wherein the substance supply unit is configured to be actuatable to supply a substance at a predeterminable pressure.

9. The delivery device of claim 6 or 7, wherein the substance supply unit is configured to be actuatable to supply a substance at a predeterminable flow rate.

10. The delivery device of claim 6 or 7, wherein the substance supply unit is configured to be actuatable to supply a substance at one or both of a predeterminable pressure and a predeterminable flow rate.

11. The delivery device of any of claims 1 to 10, wherein the delivery unit further includes a mouthpiece through which the subject in use exhales.

12. The delivery device of claim 11, wherein the delivery unit further includes a flow channel fluidly connecting the nosepiece and the mouthpiece, whereby exhaled air from an exhalation breath is delivered through the nosepiece.

13. The delivery device of any of claims 1 to 11, wherein the delivery unit further includes a flow channel fluidly connected to the nosepiece through which a gas flow, separate to an exhaled air flow

from an exhalation breath of a subject, is in use delivered, and a gas supply unit for supplying a gas flow to the flow channel.

14. The delivery device of any of claims 1 to 13, wherein the substance supply unit includes a dosing unit for supplying a substance.

15. The delivery device of claim 14, wherein the dosing unit comprises a nebulizer for supplying an aerosol.

16. The delivery device of claim 14, wherein the dosing unit comprises an aerosol canister for supplying an aerosol.

17. The delivery device of claim 14, wherein the dosing unit comprises a delivery pump unit for supplying an aerosol.

18. The delivery device of claim 17, wherein the dosing unit comprises a liquid pump unit for supplying a liquid aerosol.

19. The delivery device of claim 17, wherein the dosing unit comprises a powder pump unit for supplying a powder aerosol.

20. The delivery device of claim 14, wherein the dosing unit comprises a powder delivery unit for delivering a powder aerosol.

21. A nasal delivery device for delivering a flow entraining a substance to a nostril of a subject, including:
a nosepiece for fitting to a nostril of a subject; and
a flow resistor upstream of the outlet of the nosepiece to provide a predeterminable flow resistance to the delivered flow.

22. The delivery device of claim 21, wherein the flow resistor is a progressive resistor for progressively providing an increasing flow resistance to the delivered flow.

23. The delivery device of claim 21, wherein the flow resistor is a fixed resistor for providing a predeterminable resistance to the delivered flow.

24. The delivery device of any of claims 21 to 23, further including:
a substance supply unit which is actuatable to supply a substance.

25. The delivery device of claim 24, wherein the substance supply unit is configured to be actuatable to supply a substance at a predeterminable pressure.

26. The delivery device of claim 24, wherein the substance supply unit is configured to be actuatable to supply a substance at a predeterminable flow rate.

27. The delivery device of claim 24, wherein the substance supply unit is configured to be actuatable to supply a substance at one or both of a predeterminable pressure and a predeterminable flow rate.

28. The delivery device of any of claims 21 to 27, further including:

a mouthpiece through which the subject in use exhales.

29. The delivery device of claim 28, further including:
a flow channel fluidly connecting the nosepiece and the mouthpiece, whereby exhaled air from an exhalation breath is delivered through the nosepiece.

30. The delivery device of any of claims 21 to 29, further including:
a flow channel fluidly connected to the nosepiece through which a gas flow, separate to an exhaled air flow from an exhalation breath of a subject, is in use delivered; and
a gas supply unit for supplying a gas flow to the flow channel.

31. The delivery device of any of claims 21 to 30, wherein the substance supply unit includes a dosing unit for supplying a substance.

32. The delivery device of claim 31, wherein the dosing unit comprises a nebulizer for supplying an aerosol.

33. The delivery device of claim 31, wherein the dosing unit comprises an aerosol canister for supplying an aerosol.

34. The delivery device of claim 31, wherein the dosing unit comprises a delivery pump unit for supplying an aerosol.

35. The delivery device of claim 34, wherein the dosing unit comprises a liquid pump unit for supplying a liquid aerosol.

36. The delivery device of claim 34, wherein the dosing unit comprises a powder pump unit for supplying a powder aerosol.

37. The delivery device of claim 31, wherein the dosing unit comprises a powder delivery unit for delivering a powder aerosol.

38. A method of delivering a substance to a nasal cavity of a subject, comprising the steps of:
delivering a flow entraining a substance to one nostril of a subject; and
progressively providing an increasing flow resistance to the delivered flow.

39. The method of claim 38, further comprising the step of:
decreasing the flow resistance on development of a predeterminable pressure.

40. A method of delivering a flow entraining a substance to a nostril of a subject, comprising the steps of:
delivering a flow entraining a substance to a nostril of a subject; and
providing a predeterminable flow resistance to the delivered flow.

41. The method of claim 40, wherein the step of providing a predeterminable flow resistance to the delivered flow comprises the step of:
progressively providing an increasing flow resistance to the delivered flow.

42. The method of claim 40, wherein the step of providing a predeterminable flow resistance to the delivered flow comprises the step of:
providing a predeterminable resistance to the delivered flow.

43. A nasal delivery device for delivering a substance to a nasal cavity of a subject substantially as hereinbefore described with reference to any of Figures 1 to 3, Figures 1, 4 and 5, optionally taken in conjunction with Figure 6, of the accompanying drawings.

44. A nasal delivery device for delivering a flow entraining a substance to a nostril of a subject substantially as hereinbefore described with reference to any of Figures 7 and 8, Figures 8 and 9, Figures 8 and 10 or Figures 11 and 12 of the accompanying drawings.

45. A method of delivering a substance to a nasal cavity of a subject substantially as hereinbefore described with reference to any of Figures 1 to 3, Figures 1, 4 and 5, optionally taken in conjunction with Figure 6, of the accompanying drawings.

46. A method of delivering a flow entraining a substance to a nostril of a subject substantially as hereinbefore described with reference to any of Figures 7 and 8, Figures 8 and 9, Figures 8 and 10 or Figures 11 and 12 of the accompanying drawings.

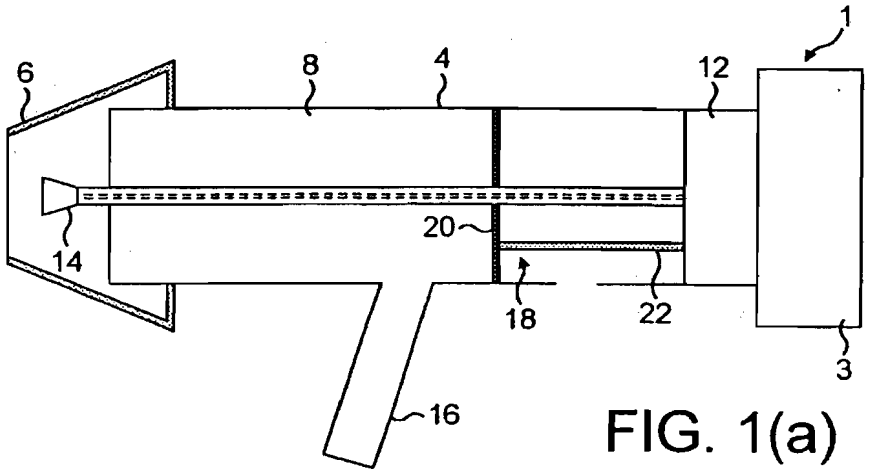


FIG. 1(a)

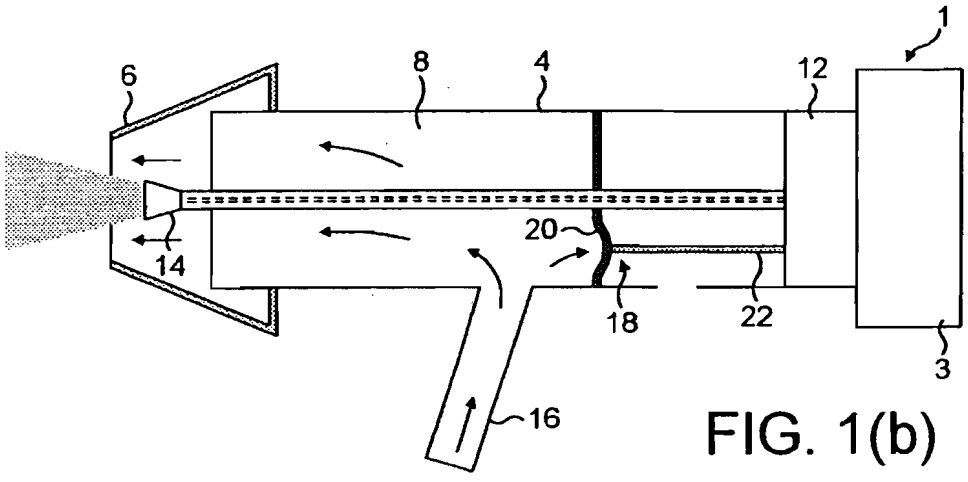


FIG. 1(b)

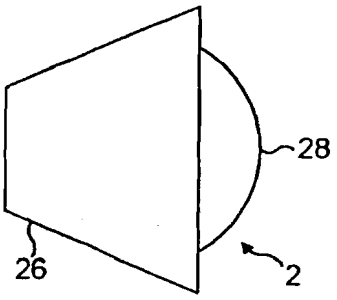


FIG. 2(a)

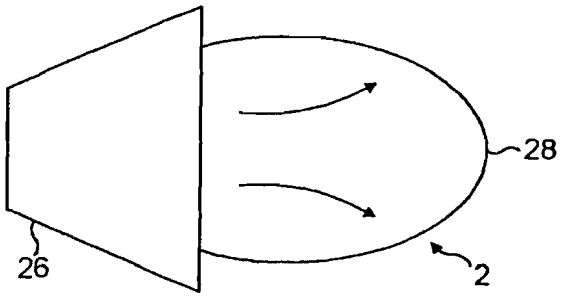


FIG. 2(b)

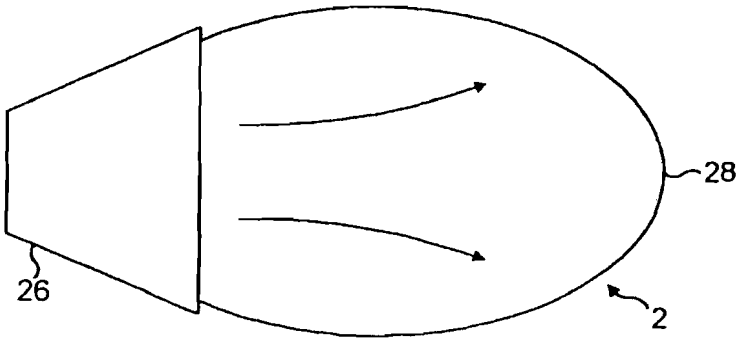


FIG. 2(c)

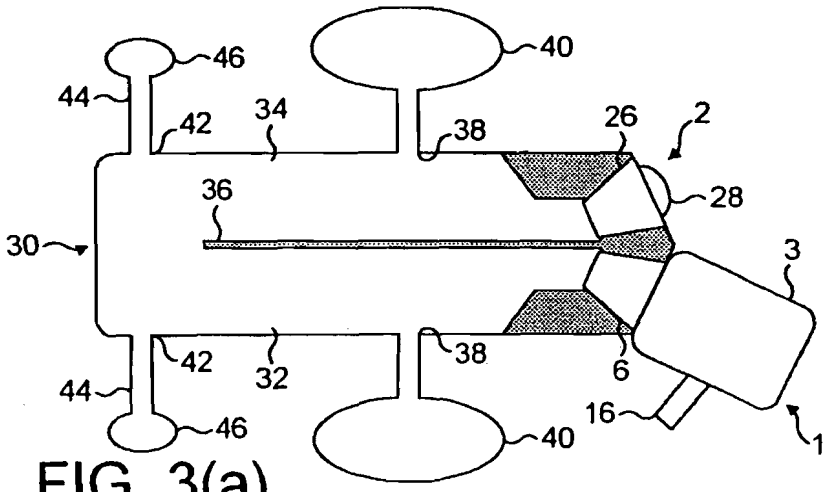


FIG. 3(a)

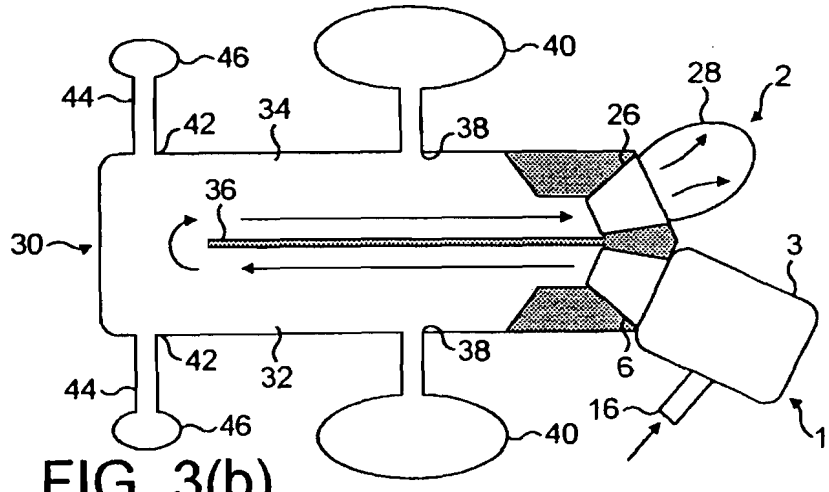


FIG. 3(b)

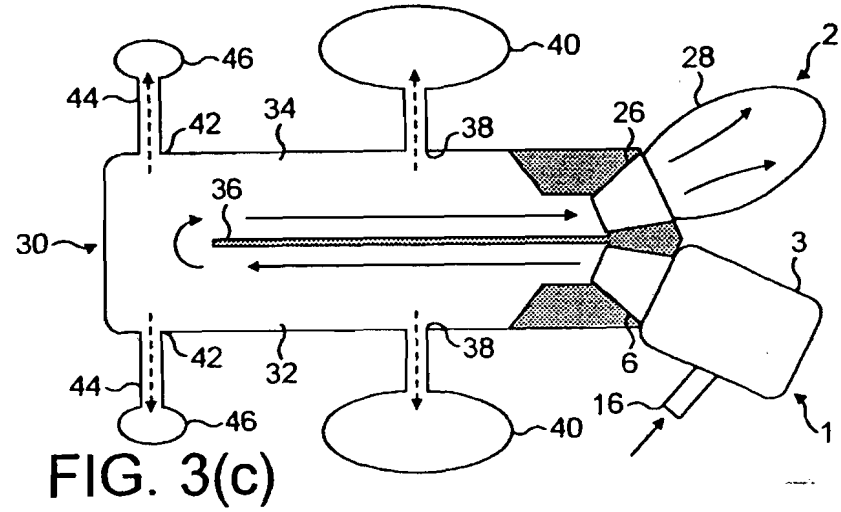


FIG. 3(c)

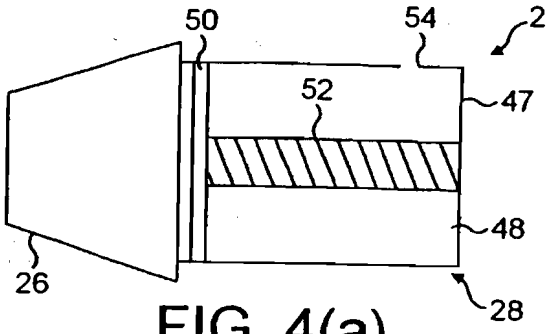


FIG. 4(a)

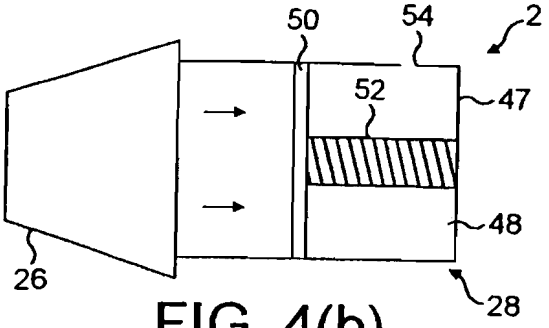


FIG. 4(b)

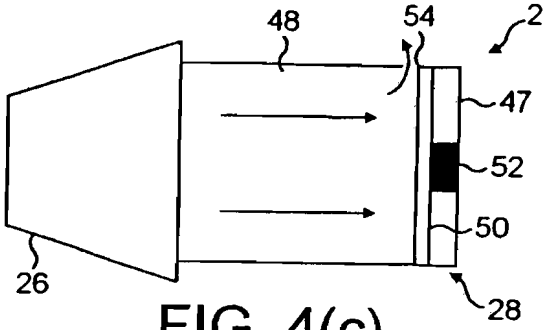


FIG. 4(c)

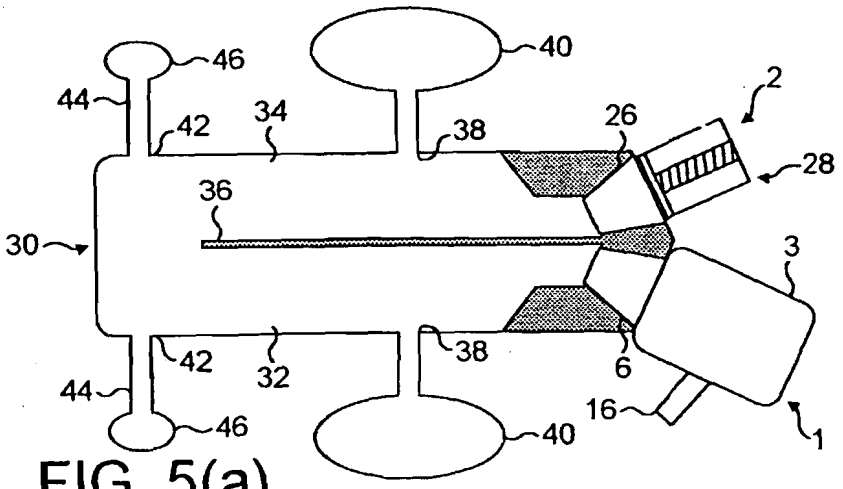


FIG. 5(a)

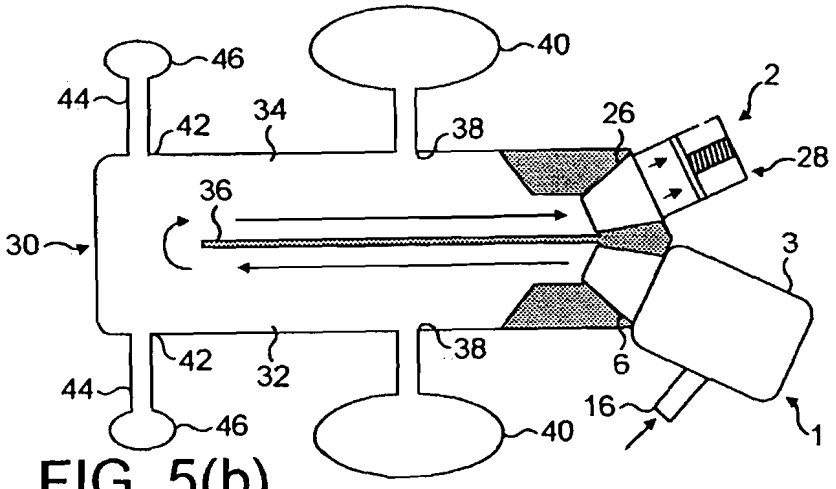


FIG. 5(b)

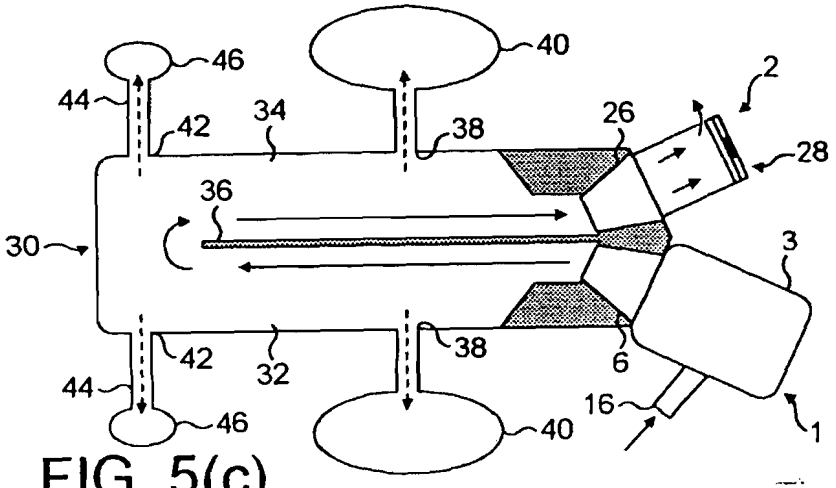


FIG. 5(c)

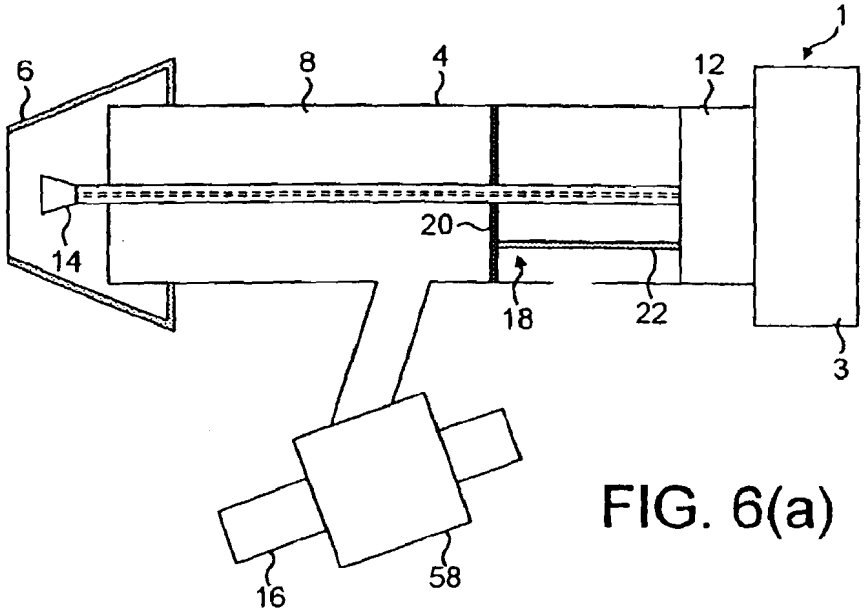


FIG. 6(a)

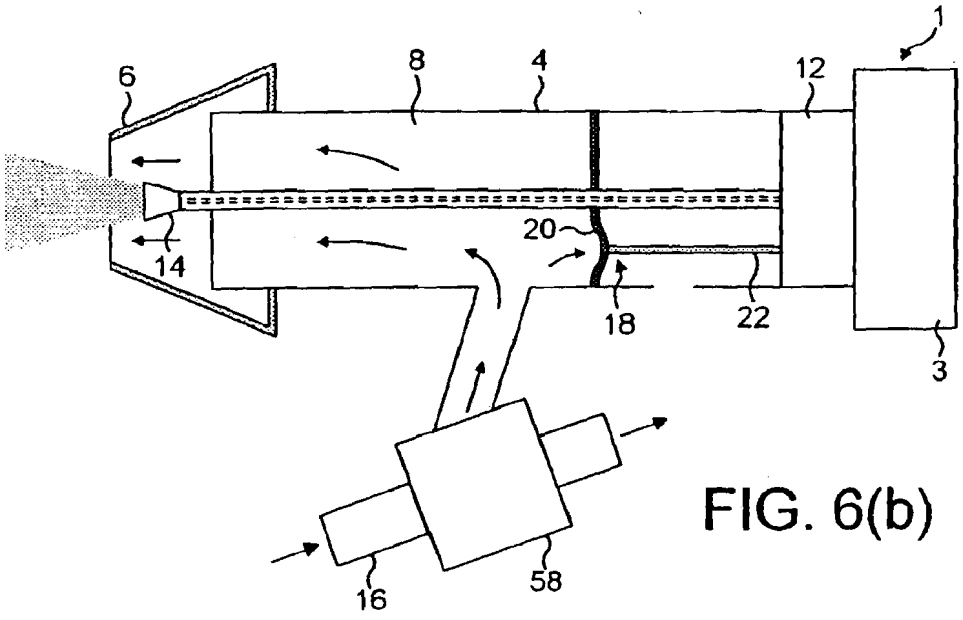


FIG. 6(b)

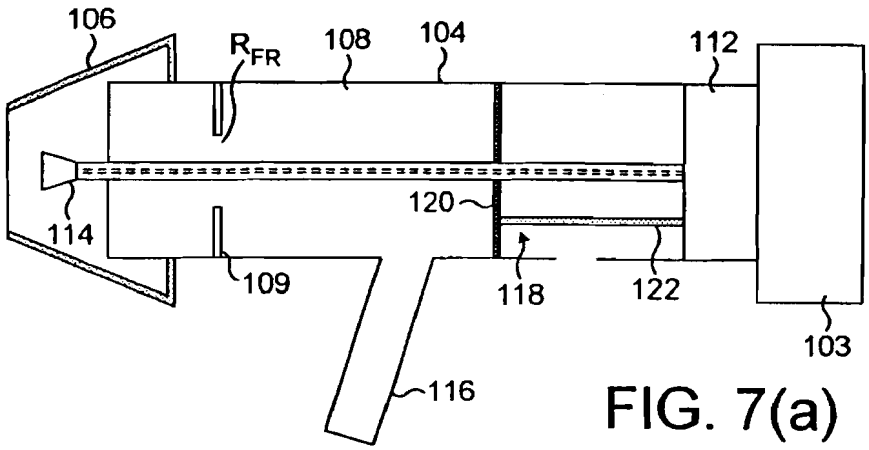

106
R_{FR}
108
104
112
120
114
109
118
122
103
116

FIG. 7(a)

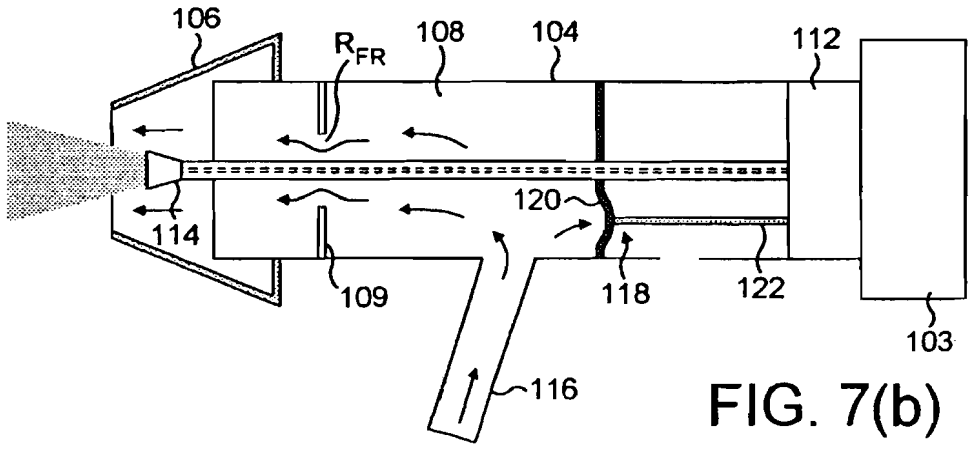

106
R_{FR}
108
104
112
120
114
109
118
122
103
116

FIG. 7(b)

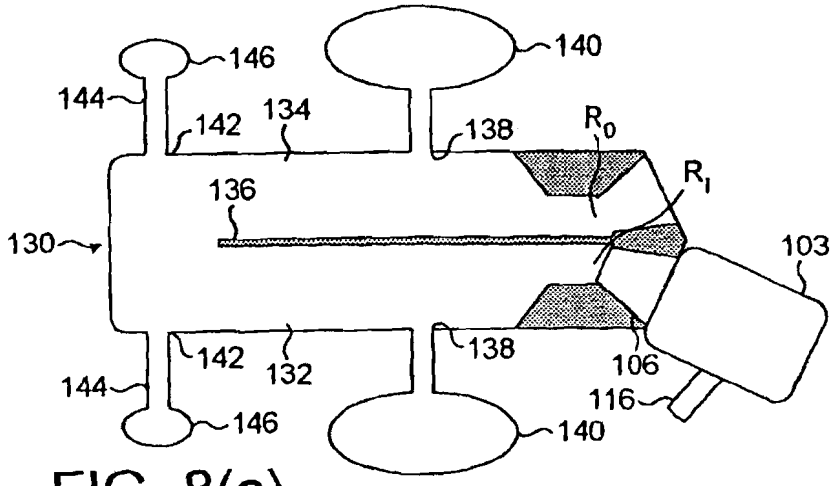

146
140
144
142
134
138
R_0
R_1
136
130
103
142
132
138
106
144
116
146
140

FIG. 8(a)

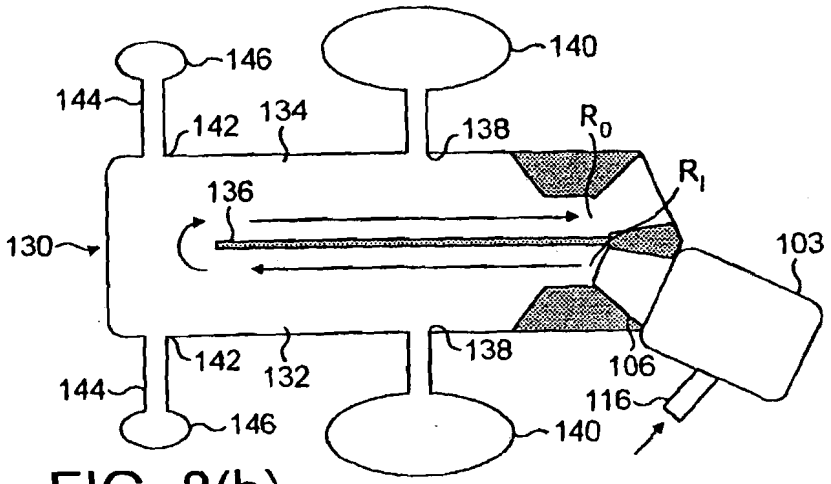
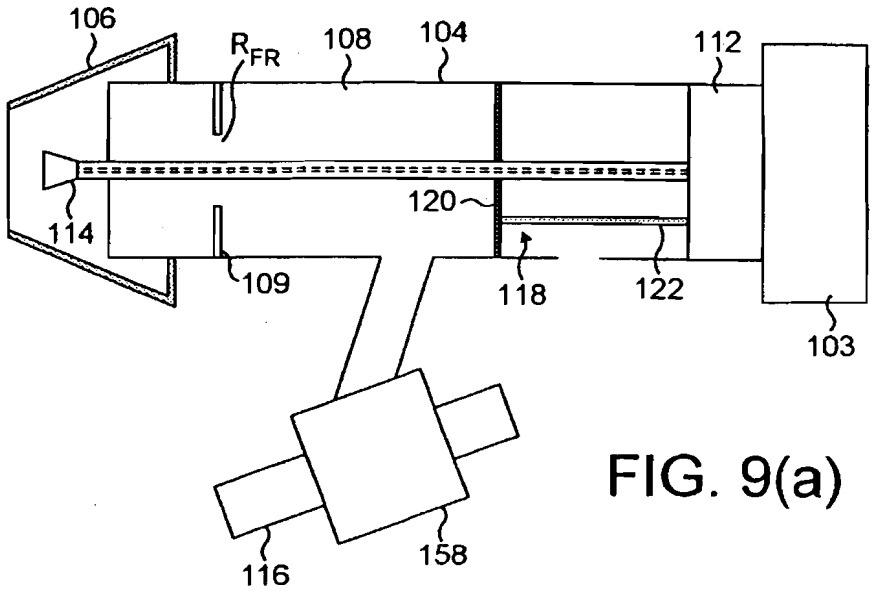

146
140
144
142
134
138
R_0
R_1
136
130
103
142
132
138
106
144
116
146
140

FIG. 8(b)


106
R_{FR}
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120
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116
158

FIG. 9(a)

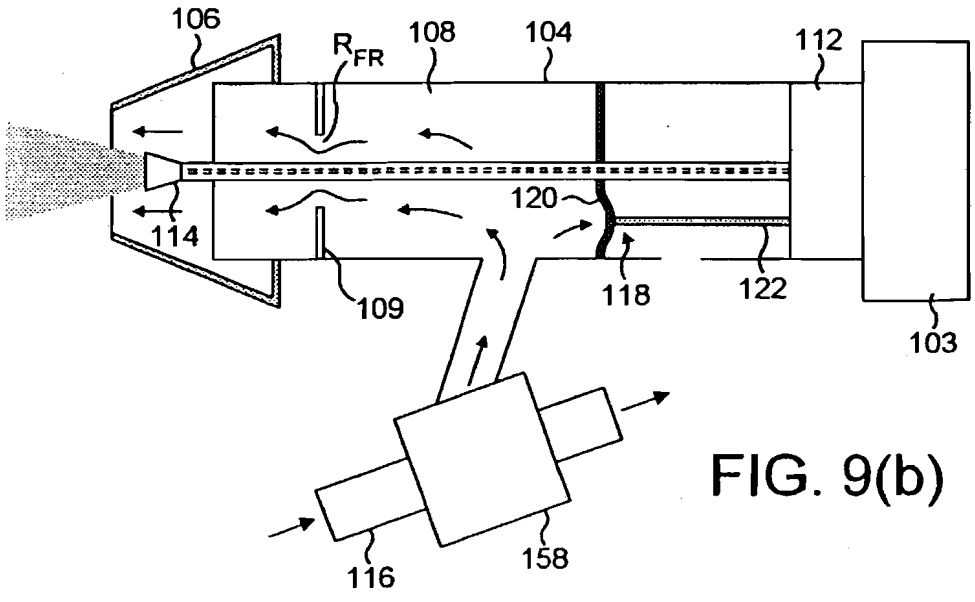
106
R_{FR}
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FIG. 9(b)

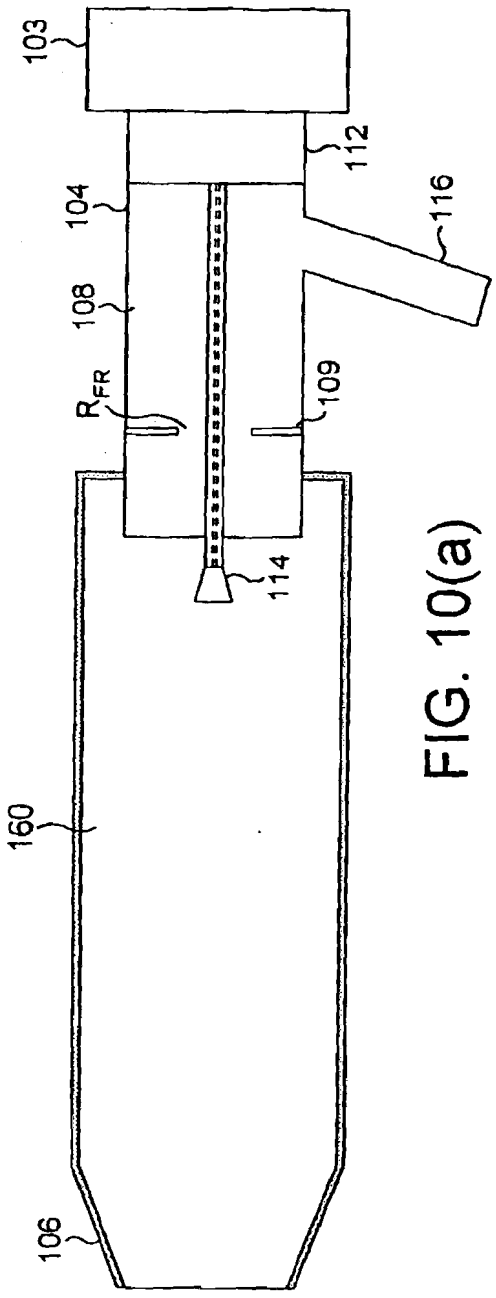

FIG. 10(a)

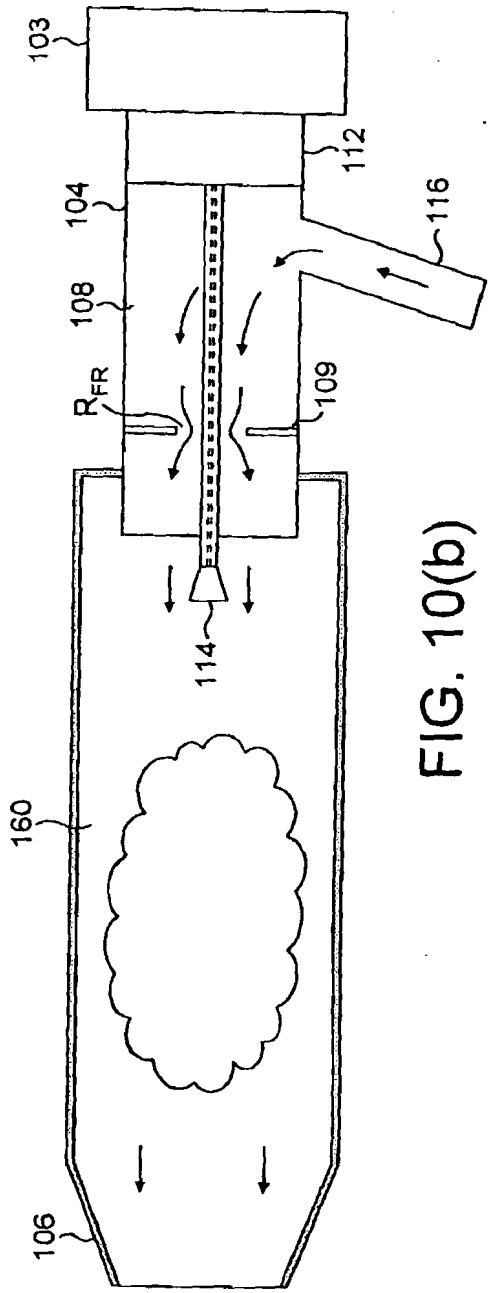

FIG. 10(b)

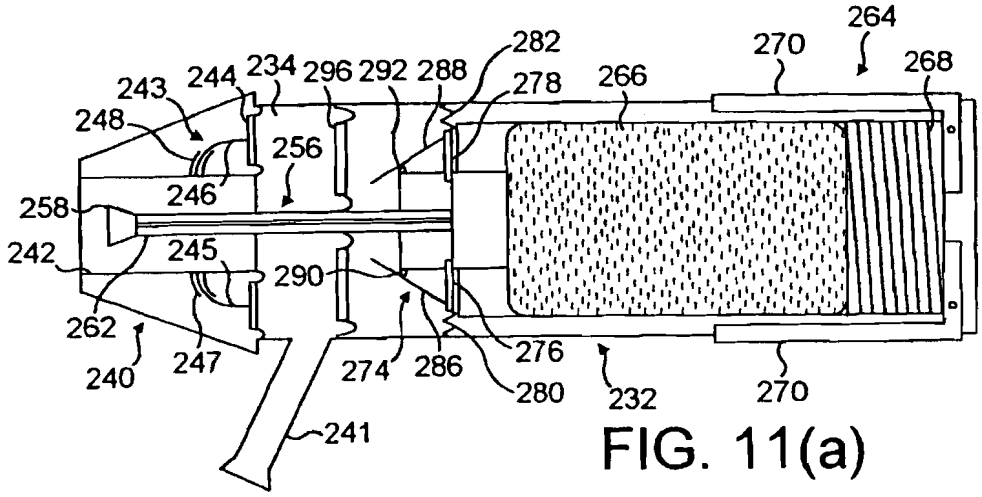

FIG. 11(a)

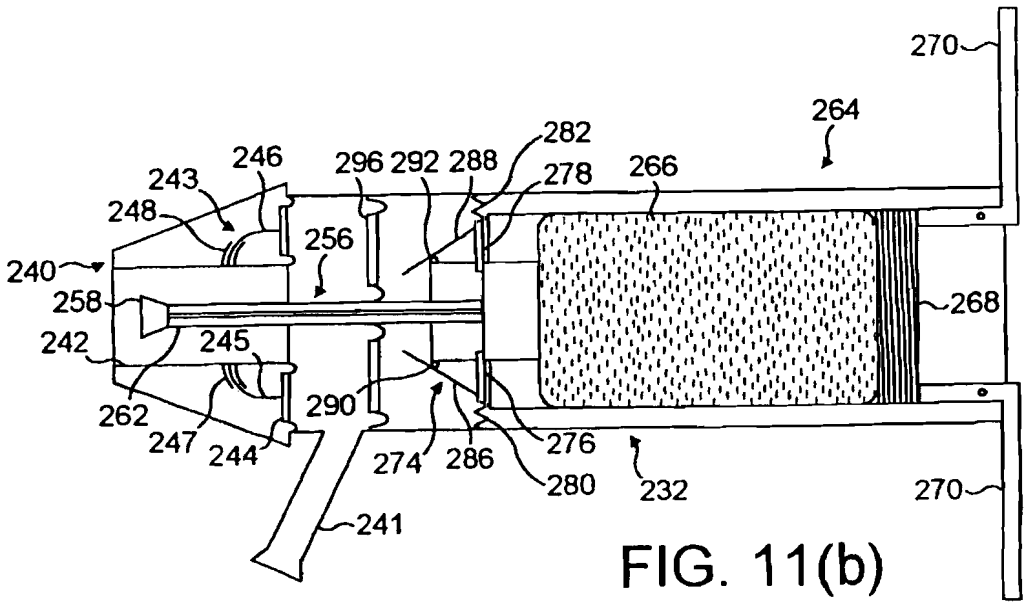

FIG. 11(b)

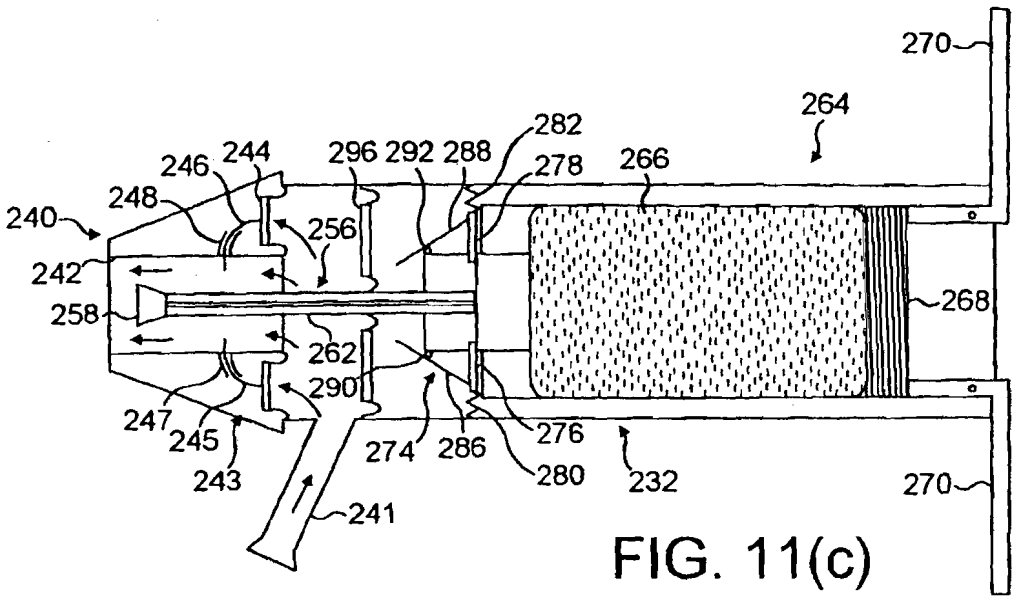

FIG. 11(c)

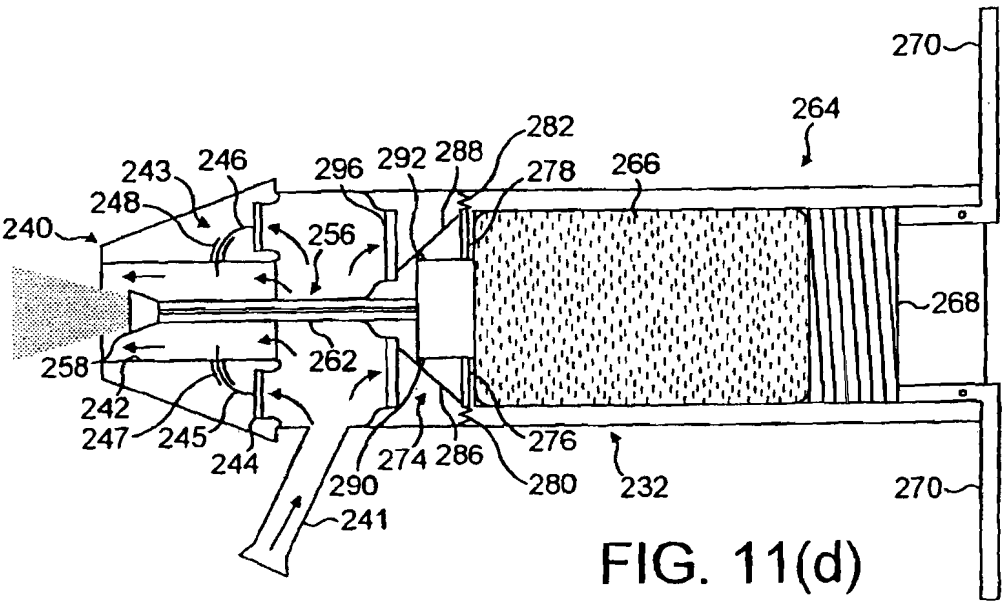

FIG. 11(d)

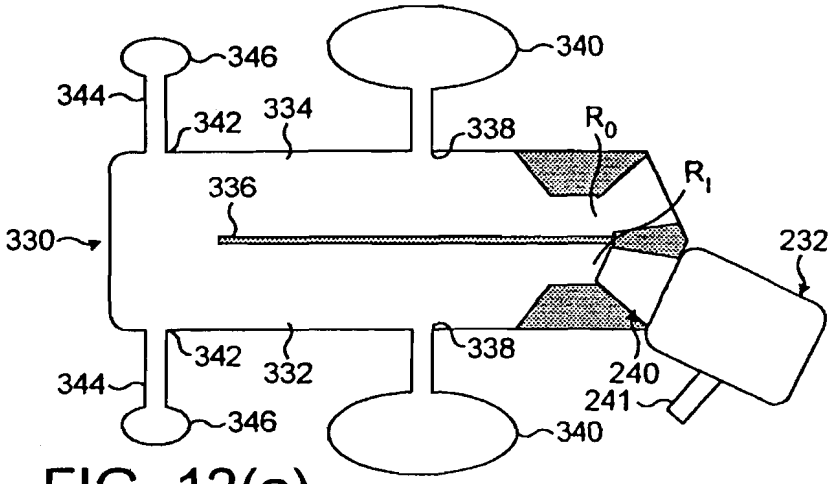

FIG. 12(a)

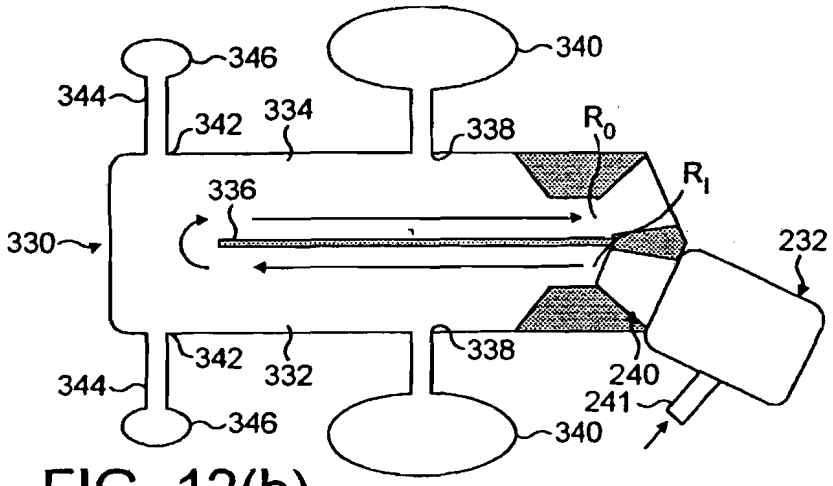

FIG. 12(b)

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(30) Priority Data:
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(71) Applicant *(for all designated States except US)*: **OPTINOSE AS** [NO/NO]; Lokkaskogen 18c, N-0773 Oslo (NO).

(72) Inventor; and
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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
12 December 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/068029 A3

(54) Title: NASAL DELIVERY DEVICES

(57) Abstract: A nasal delivery device for and a method of delivering a substance to a nasal cavity of a subject, the delivery device comprising: a delivery unit (1) for delivering a flow entraining a substance to one nostril of a subject, the delivery unit including a nosepiece (6) for fitting to a nostril of the subject; and a flow resistor (2) unit for fitting to the other nostril of the subject, the flow resistor unit including a progressive resistor (28) for progressively providing an increasing flow resistance to the delivered flow.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/01522

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 51672 A (DJUPESLAND PER GISLE) 8 September 2000 (2000-09-08) cited in the application	21,23-37
Y	page 17, line 22 -page 18, line 2	1-3, 6-20,22
A	the whole document	4,5
Y	WO 98 53869 A (KELDMANN ERIK ;KELDMANN TROELS (DK); DIRECT HALER A S (DK); PELAEZ) 3 December 1998 (1998-12-03) page 13, line 25 -page 15, line 23 abstract; figures	1,3, 6-20,22
Y	DE 298 14 024 U (HEYDE REGINE) 8 October 1998 (1998-10-08) page 1, paragraph 2; figures	2

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 September 2002	18/09/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Valfort, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/01522

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 727 546 A (SHEPHERD MICHAEL TREVOR ET AL) 17 March 1998 (1998-03-17) abstract; figures	3,4,22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/01522

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 38-46
because they relate to subject matter not required to be searched by this Authority, namely:

Method of treatment of the human body by therapy (Art.17.2.a.i) and Rule 39.1.iv) PCT)

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 02/01522

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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			BR	0008650 A	26-12-2001
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			DE	69413989 T2	08-04-1999
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			NO	960610 A	28-03-1996
			SG	82544 A1	21-08-2001
			US	6109261 A	29-08-2000

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
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PCT

(10) International Publication Number
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(51) International Patent Classification[7]: A61M 15/00

(21) International Application Number: PCT/IB02/03849

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6 September 2002 (06.09.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0121568.0 6 September 2001 (06.09.2001) GB
PCT/IB02/03034 12 June 2002 (12.06.2002) IB

(71) Applicant *(for all designated States except US)*: **OPTINOSE AS** [NO/NO]; Lokkaskogen 18c, N-0773 Oslo (NO).

(72) Inventor; and

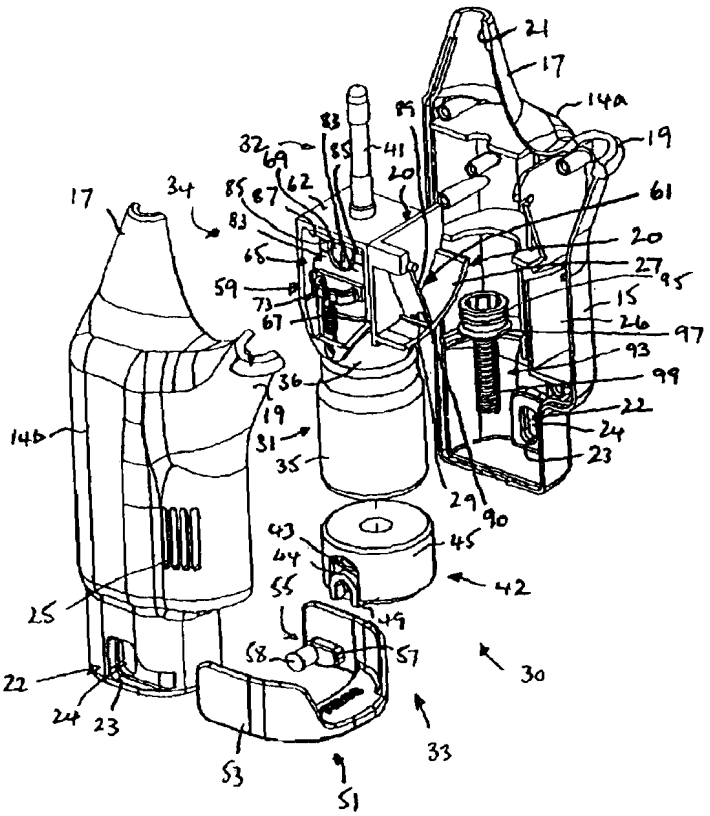
(75) Inventor/Applicant *(for US only)*: **DJUPESLAND, Per, Gisle** [NO/NO]; Lokkaskogen 18c, N-0773 Oslo (NO).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK,

[Continued on next page]

(54) Title: NASAL DELIVERY DEVICE



(57) Abstract: A breath-actuated nasal delivery device, comprising: a mouthpiece through which a user in use exhales to actuate the delivery device; a nosepiece for fitting to a nostril of the user through which a substance is in use delivered; a substance supply unit actuatable to deliver a dose of a substance through the nosepiece; a loading unit operable to load the substance supply unit with an actuation force; and a release mechanism for enabling actuation of the substance supply unit in response to exhalation by the user through the mouthpiece; wherein the release mechanism comprises a locking unit which is movable : between a locking configuration in which the substance supply unit is locked in a non- actuated position when loaded by the loading unit and a release configuration in which the substance supply unit is actuatable by the loading unit, and a trigger member for releasing the locking unit from the locking configuration to the release configuration in response to exhalation by the user through the mouthpiece and thereby enabling actuation of the substance supply unit.

WO 03/020350 A1

TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

NASAL DELIVERY DEVICE

The present invention relates to a breath-actuated nasal delivery device for and a method of delivering a substance, in particular one of a liquid, as a suspension or solution, or a powder containing a medicament, especially systemic or topical pharmaceuticals, or a vaccine to the nasal airway of a subject.

Referring to Figure 1, the nasal airway 1 comprises the two nasal cavities separated by the nasal septum, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 3 and the tubal ostia 5, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx 7, the oral cavity 9 and the lower airway 11, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx 7 and the oral cavity 9 by opening and closing of the oropharyngeal velum 13. The velum 13, which is often referred to as the soft palate, is illustrated in solid line in the closed position, as achieved by providing a certain positive pressure in the oral cavity 9, such as achieved on exhalation through the oral cavity 9, and in dashed line in the open position.

There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and

antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitionin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa advantageously provides for rapid systemic uptake.

Nasal delivery is also expected to be advantageous for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

It is also expected that nasal delivery could provide an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

Furthermore, it is expected that nasal delivery using the nasal delivery technique of the present invention will prove effective in the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of

the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

Also, it is expected that the nasal delivery technique of the present invention will allow for the effective delivery of vaccines.

Aside from the delivery of medicaments, the irrigation of the nasal mucosa with liquids, in particular saline solutions, is commonly practised to remove particles and secretions, as well as to improve the mucociliary activity of the nasal mucosa. These solutions can be used in combination with active pharmaceuticals.

For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse affects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

To date, nasal medicaments have been primarily delivered as drops or by mechanical nasal spray pumps. With mechanical spray pumps, the mean particle size is typically between 40 μm and 80 μm in order to prevent the inhalation of delivered particles. In general, particles smaller than 10 μm will bypass the nose and can be inhaled. Indeed, the new FDA guidelines require that the fraction of particles less than 10 μm be at most 5 %.

Whilst the provision of a spray having a larger mean particle size prevents the inhalation of the particles, these larger particles are not optimal for achieving a good distribution to the nasal mucosa.

The applicant has now recognized that the closure of the oropharyngeal velum during the delivery of a substance to the nasal airway prevents the possible inhalation of the substance, thereby enabling the delivery of an aerosol having a much smaller mean particle size than achieved by traditional nasal spray pumps. In this way, an aerosol can be generated which has an optimal particle size distribution.

A further advantage is that the nosepiece acts to expand the narrowest, anterior part of the nasal cavity and thereby reduces the unwanted high deposition in the anterior region of the nasal cavity which is lined by squamous epithelium.

In addition, the applicant has recognized that, by establishing a bi-directional flow through the nasal cavities as described in WO-A-00/51672, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril, an aerosol having an optimal flow rate and timing can be generated. Furthermore, the bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

A yet further advantage is that the air flow acts to create a positive pressure inside the nasal passages connected in series, which tends to expand and widen narrow and congested regions.

A still yet further advantage is that the two-point fixation of the device in the nose with a well-fitting nozzle and in the mouth provides a much more stable and reproducible positioning of the device as compared to traditional spray pumps. Thus, in addition to improved deposition and reproducibility, the new concept provides a more user-friendly and intuitive nasal delivery method.

Furthermore, the delivery device, in being pre-primed and actuatable by the oral exhalation breath of a subject, does not require the application of an actuation force by the subject at the time of actuation. Traditionally, mechanical liquid delivery pumps are operated by the manual compression of a chamber containing a volume of liquid to expel a flow of a metered volume of liquid, and mechanical powder delivery pumps are operated by the manual compression of a chamber containing a volume of air to drive and expel a flow of a metered amount of a dry powder. Such operation requires a relatively high actuation force, typically of the order of 50 N, which high force often leads to significant movement of the delivery device, it being very difficult to maintain a delivery device stationary when attempting to apply a high actuation force. Movement of the delivery device, both in the positioning and orientation of the nozzle, will lead to poor reproducibility, dose accuracy and patient compliance. In being pre-primed and actuatable by the oral exhalation breath of a subject, the delivery device of the present invention overcomes this problem.

In addition, by not requiring a subject to apply an actuation force at the instance of delivery, the delivery device provides for the same actuation force in each delivery, and also provides for delivery at an optimal pressure and/or flow rate, and the delivery of substance having an optimized particle size distribution.

Yet furthermore, in providing for the closure of the oropharyngeal velum of a subject, substance is prevented from entering the lower airway, and also, in a preferred embodiment, bi-directional delivery can be achieved through the nasal cavities.

It will be appreciated that the nasal delivery devices of the present invention are quite different to inhalation devices which provide for inhalation into the lower airway.

Inhalation devices have been used for a long time for the inhalation of medicaments in the treatment of lower airway pathologies.

One such inhalation device is the pressurized metered dose inhaler (pMDI). In such inhalers, a metered dose of medicament is released as an aerosol by actuating an aerosol canister, with the particle sizes of the aerosol being required to be small, typically less

than 5 μm, in order to reach the distal parts of the lower airway. One drawback with traditional pMDIs is that the subject must co-ordinate inhalation with the aerosol release in order to deliver the aerosolized medicament effectively to the lower airway. Inadequate co-ordination represents a considerable problem, significantly reducing both lung deposition and reproducibility. Another drawback with traditional pMDIs is the use of chlorine-containing compounds as the propellant gas, as such gases are not environmentally friendly and have been demonstrated to destroy the ozone layer. Recently, in order to alleviate these drawbacks, pMDIs have been developed which use an alternative propellant gas, this being a hydrofluoroalkane (HFA), and incorporate a breath-actuation mechanism which provides for actuation of the aerosol canister on inhalation by the subject.

Another such inhalation device is the dry powder inhaler, such as the Turbohaler® inhaler as supplied by AstraZeneca and the Discus® inhaler as supplied by GSK. These dry powder inhalers do not require co-ordination of delivery and inhalation and can improve deposition to the lower airways.

Bi-directional nasal drug delivery is achieved by directing an exhaled air flow through the nasal passages in series, or by triggering another flow source to create such an air flow, whereas breath actuation of pulmonary drug delivery is by inhalation into a closed expanding volume, that is, the lungs. For bi-directional nasal delivery, it is desirable to establish the air flow before the drug is released, whereas for inhalation, the release is best achieved at the very beginning of inspiration to reach the most distal parts of the lungs.

Increased airway resistance in pathological conditions, both in the pulmonary and nasal airways, is a challenge. In inhalation devices, an air flow is created by the inspiratory muscles creating a negative pressure inside the chest. In this way, air is sucked through the device and into the airways. For pulmonary drug delivery, it is essential that the triggering occurs, not only early, but also at a relatively low flow to ensure release in subjects with a very low lung capacity. Furthermore, the releasing action should require as little energy as possible, as any resistance in the device will impede free inhalation.

Still most subjects, even patients with lung diseases, will be able to achieve a flow rate of 25 L/min which is typically required to trigger the release from a pMDI device.

For the nose, the situation is more complex and in many ways different. The expiratory muscles in the thorax produce the exhaled air flow used to trigger release, and this air flow is then directed through the device and into the nasal passages in series, or used to trigger another flow source. Thus, the triggering air flow is completely reversed as compared to pulmonary breath actuation, and the air flow is directed into another airway/compartment separated from the lower airways.

Furthermore, the nose geometry is designed to humidify, warm and filter the inspired air to protect the lower airways. The resistance in the nose alone equals 50 % of the total airway resistance, and the resistance may increase immensely when congested. Owing to the high anterior resistance, turbulence occurs just posterior to the constriction, increasing deposition in this region. To achieve a better distribution to larger and more posterior parts of the nasal mucosa, it is envisaged to be advantageous to have the drug released at a lower flow in a congested nose and at a higher flow in a open nose. This requires a system which can be released not only by flow, but also by pressure. Such release is essential for an efficient and reliable exhalation-triggered nasal drug delivery. In this regard, reference is made to co-pending UK application nos 0104692.9 and 0114272.8, the contents of which are hereby incorporated by reference. The two main triggering modes, flow and pressure, are to certain extent overlapping. They can be incorporated in one single mechanism or provided as separate mechanisms. However, the nose may become completely blocked, in particular during colds and allergic attacks. In this situation, it becomes impossible to establish a bi-directional air flow, but still it is desirable and necessary to deliver drugs to the nose. Furthermore, for some purposes, the exhaled air flow may only be used to trigger release from a pMDI or a mechanical spray pump. Again, the triggering may be mainly flow dependent or mainly/strictly pressure dependent.

Thus, the requirements for a breath-actuation mechanism for nasal drugs are different from those for inhaled drugs. The main features of exhalation-triggered nasal drug release are (i) triggering of drug release by exhalation, (ii) triggering when a bi-

directional flow is established, (iii) triggering at a flow rate which provides optimal distribution, (iv) triggering in a very congested and even completely blocked nose, (v) triggering of external flow sources (pMDI), and (vii) triggering of a spray pump aerosol even in the absence of bi-directional flow.

In one aspect the present invention provides a breath-actuated nasal delivery device, comprising: a mouthpiece through which a user in use exhales to actuate the delivery device; a nosepiece for fitting to a nostril of the user through which a substance is in use delivered; a substance supply unit actuatable to deliver a dose of a substance through the nosepiece; a loading unit operable to load the substance supply unit with an actuation force; and a release mechanism for enabling actuation of the substance supply unit in response to exhalation by the user through the mouthpiece; wherein the release mechanism comprises a locking unit which is movable between a locking configuration in which the substance supply unit is locked in a non-actuated position when loaded by the loading unit and a release configuration in which the substance supply unit is actuatable by the loading unit, and a trigger member for releasing the locking unit from the locking configuration to the release configuration in response to exhalation by the user through the mouthpiece and thereby enabling actuation of the substance supply unit.

In one embodiment the trigger member comprises a flow-sensitive element in fluid communication with the mouthpiece.

In one embodiment the flow-sensitive element comprises a vane.

Preferably, the flow-sensitive element includes an aperture which allows for a predeterminable air flow thereover prior to actuation.

Preferably, the flow-sensitive element is one or both of shaped and sized such as to allow for a predeterminable air flow thereover prior to actuation.

In another embodiment the trigger member comprises a pressure-sensitive element in fluid communication with the mouthpiece.

In one embodiment the pressure-sensitive element comprises a vane.

In another embodiment the pressure-sensitive element comprises a flexible membrane.

Preferably, the flexible membrane comprises a resilient membrane.

In a further embodiment the pressure-sensitive element comprises a flexible membrane in fluid communication with the mouthpiece and a vane operable by the flexible membrane.

Preferably, the flexible membrane comprises a resilient membrane.

Preferably, the delivery device further comprises: a pressure-sensitive sealing unit disposed downstream of the trigger member and being operable to vent an air flow developed by the user on exhalation through the mouthpiece to atmosphere, the sealing unit being normally closed and operable such as to be opened on generation of a predeterminable pressure thereat.

In one embodiment the sealing unit comprises an annular seal, a sealing member movable between a closed position in sealing engagement with the annular seal and an open position in which an air flow can flow through the annular seal, and a biasing element for normally biasing the sealing member to the closed position and enabling the sealing member to be opened on generation of a predeterminable pressure thereat.

In another embodiment the sealing unit comprises a flexible membrane which is movable between a closed position and an open position in which an air flow can flow thereby.

Preferably, the flexible membrane comprises a resilient membrane.

Preferably, the trigger member includes a pivot pin about which the same is rotatable, which pivot pin is engaged by the locking unit when in the locking configuration such

that the locking unit is moved from the locking configuration to the release configuration on rotation of the pivot pin.

More preferably, the locking unit includes a first, support member which abuts the substance supply unit in the locking configuration and a second, link member which engages the pivot pin of the trigger member in the locking configuration, wherein the link member is movable in relation to the support member and configured to be moved on rotation of the pivot pin to move the locking unit from the locking configuration to the release configuration.

Yet more preferably, the link member is rotatably connected to the support member.

Still more preferably, the link member is configured to load the pivot pin radially.

In one embodiment the delivery device further comprises: a flow path fluidly connecting the nosepiece and the mouthpiece, whereby an air flow developed by exhalation by the user through the mouthpiece is delivered through the nosepiece.

In another embodiment the nosepiece and the mouthpiece are fluidly isolated such that an air flow developed by exhalation by the user through the mouthpiece is not delivered through the nosepiece.

In one embodiment the substance supply unit comprises a nebulizer for supplying an aerosol.

In another embodiment the substance supply unit comprises an aerosol canister for supplying an aerosol.

In a further embodiment the substance supply unit comprises a delivery pump unit for supplying one of an aerosol or a jet.

In one preferred embodiment the delivery pump unit comprises a liquid pump unit for supplying a liquid aerosol.

In another preferred embodiment the delivery pump unit comprises a powder pump unit for supplying a powder aerosol.

In a yet further embodiment the substance supply unit comprises a powder delivery unit for delivering a powder aerosol.

Preferably, the delivery device further comprises: a flow-control mechanism disposed upstream of the trigger member to at least restrict an air flow to the trigger member such as to prevent actuation of the release mechanism on exhalation by the user through the mouthpiece where the delivery device is being improperly operated.

In one embodiment the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the delivery device is in an improper orient.

In another embodiment the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the air flow developed by the user has a rate exceeding a predeterminable threshold value.

More preferably, the flow-control mechanism comprises a flow channel section which includes a recess, and a ball which is movably, captively disposed within the flow channel section, the ball normally, with proper operation of the delivery device, resting in the recess such as to allow a sufficient air flow to the trigger member as to enable actuation of the release mechanism, and being moved to at least partially block the flow channel section where the delivery device is being improperly operated such as to prevent actuation of the release mechanism.

In another aspect the present invention provides a breath-actuated nasal delivery device, comprising: a mouthpiece through which a user in use exhales to actuate the delivery device; a nosepiece for fitting to a nostril of the user through which a substance is in use delivered and being in fluid communication with the mouthpiece; a substance supply unit actuatable to deliver a dose of a substance through the nosepiece; a release mechanism for enabling actuation of the substance supply unit in response to exhalation

by the user through the mouthpiece; and a flow-control mechanism disposed upstream of the trigger member to at least restrict an air flow to the trigger member such as to prevent actuation of the release mechanism on exhalation by the user through the mouthpiece where the delivery device is being improperly operated.

In one embodiment the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the delivery device is in an improper orient.

In another embodiment the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the air flow developed by the user has a rate exceeding a predeterminable threshold value.

Preferably, the flow-control mechanism comprises a flow channel section which includes a recess, and a ball which is movably, captively disposed within the flow channel section, the ball normally, with proper operation of the delivery device, resting in the recess such as to allow a sufficient air flow to the trigger member as to enable actuation of the release mechanism, and being moved to at least partially block the flow channel section where the delivery device is being improperly operated such as to prevent actuation of the release mechanism.

In a further aspect the present invention provides a release mechanism for enabling actuation of a substance supply unit, the release mechanism comprising: a locking unit which is movable between a locking configuration in which the substance supply unit is locked in a non-actuated position and a release configuration in which the substance supply unit is actuatable; and a trigger member for releasing the locking unit from the locking configuration to the release configuration in response to a gas flow thereat, wherein the trigger member includes a pivot pin about which the same is rotatable, which pivot pin is engaged by the locking unit when in the locking configuration such that the locking unit is moved from the locking configuration to the release configuration on rotation of the pivot pin.

Preferably, the locking unit includes a first, support member which abuts the substance supply unit in the locking configuration and a second, link member which engages the

pivot pin of the trigger member in the locking configuration, wherein the link member is movable in relation to the support member and configured to be moved on rotation of the pivot pin to move the locking unit from the locking configuration to the release configuration.

Preferably, the link member is rotatably connected to the support member.

Preferably, the link member is configured to load the pivot pin radially.

In a still further aspect the present invention provides a breath-actuated nasal delivery pump for delivering a liquid containing a substance to a nasal cavity of a user.

In one embodiment the delivery pump is a spray pump and the liquid is delivered as a liquid spray.

In another embodiment the delivery pump is a jet pump and the liquid is delivered as a liquid jet.

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figure 1 schematically illustrates the anatomy of the upper respiratory tract of a human subject;

Figure 2(a) illustrates a perspective view of a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 2(b) illustrates one side view of the nasal delivery device of Figure 2(a);

Figure 2(c) illustrates another side view of the nasal delivery device of Figure 2(a);

Figure 2(d) illustrates a plan view of the nasal delivery device of Figure 2(a);

Figure 3 illustrates a part-exploded perspective view of the nasal delivery device of Figure 2(a);

Figure 4(a) illustrates one side view of the substance delivery assembly of the nasal delivery device of Figure 2(a);

Figure 4(b) illustrates another side view of the substance delivery assembly of the nasal delivery device of Figure 2(a);

Figure 4(c) illustrates a part-sectional other side view of the substance delivery assembly of the nasal delivery device of Figure 2(a);

Figure 4(d) illustrates an exploded perspective view of the substance delivery assembly of the nasal delivery device of Figure 2(a);

Figure 5(a) illustrates a side view of the loading unit of the loading mechanism of the substance delivery assembly of the nasal delivery device of Figure 2(a);

Figure 5(b) illustrates a vertical sectional view through the loading unit of Figure 5(a);

Figure 5(c) illustrates an exploded side view of the loading unit of Figure 5(a);

Figure 6(a) illustrates a side view of the pressure-sensitive release mechanism of the nasal delivery device of Figure 2(a);

Figure 6(b) illustrates a vertical sectional view of the pressure-sensitive release mechanism of Figure 6(a);

Figure 6(c) illustrates an exploded perspective view of the pressure-sensitive release mechanism of Figure 6(a);

Figure 7(a) illustrates a part cut-away perspective view of the nasal delivery device of Figure 2(a) in an inoperative, rest configuration;

Figure 7(b) illustrates a part cut-away perspective view of the nasal delivery device of Figure 2(a) in a loaded, operable configuration;

Figure 7(c) illustrates a part cut-away perspective view of the nasal delivery device of Figure 2(a) where operated in one mode of operation;

Figure 7(d) illustrates a part cut-away perspective view of the nasal delivery device of Figure 2(a) where operated in another mode of operation;

Figure 8(a) illustrates a part-sectional view of a nasal delivery device in accordance with a second embodiment of the present invention, illustrated in an inoperative, rest configuration;

Figure 8(b) illustrates a part-sectional view of the nasal delivery device of Figure 8(a) in a loaded, operable configuration;

Figure 8(c) illustrates a part-sectional view of the nasal delivery device of Figure 8(a) in an actuated configuration;

Figure 9(a) illustrates in enlarged scale region A of Figure 8(a);

Figure 9(b) illustrates in enlarged scale region B of Figure 8(c);

Figure 10(a) illustrates a part-sectional view of a nasal delivery device in accordance with a third embodiment of the present invention, illustrated in an inoperative, rest configuration;

Figure 10(b) illustrates a part-sectional view of the nasal delivery device of Figure 10(a) in a loaded, operable configuration;

Figure 10(c) illustrates a part-sectional view of the nasal delivery device of Figure 10(a) in an actuated configuration;

Figure 11(a) illustrates in enlarged scale region C of Figure 10(a);

Figure 11(b) illustrates in enlarged scale region D of Figure 10(c);

Figure 12(a) illustrates a part-sectional view of a nasal delivery device in accordance with a fourth embodiment of the present invention, illustrated in an inoperative, rest configuration;

Figure 12(b) illustrates a part-sectional view of the nasal delivery device of Figure 12(a) in a loaded, operable configuration;

Figure 12(c) illustrates a part-sectional view of the nasal delivery device of Figure 12(a) in an actuated configuration;

Figure 13(a) illustrates in enlarged scale region E of Figure 12(a);

Figure 13(b) illustrates in enlarged scale region F of Figure 12(c);

Figures 14(a) and (b) illustrate a flow-control mechanism in accordance with an embodiment of the present invention; and

Figures 15(a) to (c) illustrate the function of the flow-control mechanism of Figures 14(a) and (b) where a user exhales rapidly or inhales therethrough.

Figures 2 to 7 illustrate a breath-actuated nasal delivery device in accordance with a first embodiment of the present invention.

The delivery device comprises a housing unit 14, in this embodiment provided by first and second housing parts 14a, 14b, which defines a main body 15 which is typically gripped in the hand of a user, a nosepiece 17 for fitting to a nostril of a user and a mouthpiece 19 through which the user exhales to actuate the delivery device, and a

guide member 20 which, in this embodiment, together with the housing unit 14 defines a main flow path 21 between the nosepiece 17 and the mouthpiece 19.

The main body 15 includes first and second cam recesses 22, 22 on opposed sides at a lower end thereof for receiving respective ones of the engagement elements 55, 55 of a loading member 51, as will be described in more detail hereinbelow. The cam recesses 22, 22 each comprise a cam surface 23 which engages the cam element 57 of a respective one of the engagement elements 55, 55 of the loading member 51, and a lug aperture 24 adjacent the cam surface 23 through which extends the lug 58 of the respective one of the engagement elements 55, 55 of the loading member 51.

The main body 15 includes at least one external venting aperture, in this embodiment a plurality of external venting apertures 25, 25 which provide for a vent to atmosphere, and further defines a gas venting path 26 which can provide a fluid communication path between the external venting apertures 25, 25 and the main flow path 21 at a location downstream of the vane 89 of a trigger member 61, as will be described in more detail hereinbelow. As will be described in more detail hereinbelow, the gas venting path 26 is normally isolated from the main flow path 21 by a pressure-sensitive sealing unit 93, and is brought into fluid communication with the main flow path 21 by opening the pressure-sensitive sealing unit 93 where a sufficient flow rate cannot be developed through the main flow path 21, for example, as a result of the nasal passage of the user being congested, and the pressure in the main flow path 21 exceeds a predetermined threshold pressure.

In this embodiment the nosepiece 17 has a tapering section which narrows to the distal end thereof and acts, when inserted, typically from about 1 to 2 cm, into the anterior part of a nasal cavity, to expand the narrow nasal valve of the nasal cavity and provide a fluid-tight seal.

In this embodiment the mouthpiece 19 is configured to be gripped in the lips of a user. In an alternative embodiment the mouthpiece 19 could be configured to be gripped by the teeth of a user and sealed by the lips of the user. In a preferred embodiment the mouthpiece 19 is specifically configured to have one or both of a shape and geometry

which allows the delivery device to be gripped repeatedly in the same position, thereby providing for the nosepiece 17 to be reliably inserted in the same position in the nasal cavity.

The guide member 20 includes an arcuate section 27, adjacent which the distal end of the vane 89 of the trigger member 61 is movably disposed, and a vane stop 29 which defines the rest position of the vane 89 of the trigger member 61 when a locking assembly 59 is in the locking configuration. The provision of the vane stop 29 acts to prevent the actuation of a substance supply unit 31 on inhalation by the user, as will be described in more detail hereinbelow.

In this embodiment the main flow path 21 provides a fluid communication path between the nosepiece 17 and the mouthpiece 19 such that an exhalation breath of the user can provide for bi-directional flow through the nasal cavities as disclosed in WO-A-00/51672. In alternative embodiments there could be no fluid communication path between the nosepiece 17 and the mouthpiece 19 such that an exhalation breath of the user is not directed to the nasal cavities of the user. These alternative embodiments include those where substance is delivered in a separate gas flow, such as from a pressurized canister, for example, a pMDI canister.

The delivery device further comprises a breath-actuated substance delivery assembly 30 for delivering substance through the nosepiece 17 on exhalation by the user through the mouthpiece 19.

The substance delivery assembly 30 comprises a substance supply unit 31 for delivering a metered dose of a substance on actuation of the same, an outlet unit 32 which is fluidly connected to the substance supply unit 31 for delivering substance through the nosepiece 17, a loading mechanism 33 for loading the substance supply unit 31, and a release mechanism 34 for releasing the substance supply unit 31 from a loaded, non-actuated position to an actuated position on exhalation by the user through the mouthpiece 19.

In this embodiment the substance supply unit 31, as a mechanical pump, comprises a container 35 containing a volume of liquid containing a substance, a pump fitting 36

which includes a metering chamber and is connected to the container 35, and an outlet stem 37 which is movably disposed to the pump fitting 36 and through which liquid is delivered. In operation, a metered volume of liquid is delivered on relative movement of the pump fitting 36 and the outlet stem 37, in this embodiment movement of the pump fitting 36 in relation to the outlet stem 37, between a first position in which the outlet stem 37 is extended from the pump fitting 36 and a second position in which the outlet stem 37 is depressed into the pump fitting 36.

In this embodiment the substance supply unit 31 is a multi-dose device for enabling the delivery of a succession of metered doses of substance. In an alternative embodiment the substance supply unit 31 could be a single dose device for delivering a single metered dose of substance.

The outlet unit 32 comprises an outlet block 40 which is fluidly connected to the outlet stem 37 of the substance supply unit 31 and, in this embodiment, includes a valve and swirl chamber, and a delivery tube 41 from which a mist of fine droplets of the liquid is expelled on actuation of the substance supply unit 31. In an alternative embodiment the delivery tube 41 could be configured to provide for the delivery of a liquid jet.

The loading mechanism 33 comprises a loading unit 42 which comprises a biasing element 43, in this embodiment a resilient element, here a compression spring, and first and second retaining elements 44, 45 between which the biasing element 43 is disposed such as to loadable with an actuation force, which is sufficient to actuate the substance supply unit 31 when released, on compression of the same, in this embodiment by moving one, the lower, retaining element 44 relative to the other, upper, retaining element 45. In this embodiment the retaining elements 44, 45 are coupled by a link 47, here a nut and bolt, to constrain the expansion of the biasing element 43 and thereby pre-bias the biasing element 43 to a predetermined extent. In this embodiment the one, lower retaining element 44 includes first and second shoulders 49, 49 on opposed sides thereof which are engaged by the respective lugs 58, 58 of the engagement elements 55, 55 of the loading member 51, as will be described in more detail hereinbelow.

The loading mechanism 33 further comprises a loading member 51 for loading the loading unit 42. In this embodiment the loading member 51 comprises a U-shaped lever 53 which is movable from a non-loading position, as illustrated in Figure 7(a), to a loading position, as illustrated in Figure 7(b), in which the loading member 51 acts to load the loading unit 42 by biasing the same against the bottom end of the container 35 of the substance supply unit 31.

The loading member 51 includes first and second engagement elements 55, 55 which are disposed in opposed relation at the respective ends of the lever 53 and are located in respective ones of the cam recesses 22, 22 in the main body 15 of the body unit 14 and engage respective ones of the shoulders 49, 49 on the lower retaining element 44 of the loading unit 42.

The engagement elements 55, 55 each comprise a cam 57 which is located at a respective one of the cam surfaces 23, 23 of the cam recesses 22, 22 in the main body 15 of the body unit 14, and a lug 58 which extends through a respective one of the lug apertures 24, 24 of the cam recesses 22, 22 in the main body 15 of the body unit 14 and engages a respective one of the shoulders 49, 49 on the lower retaining element 44 of the loading unit 42. The cams 57, 57 are configured such that, on moving the lever 53 from the non-loading, rest position to the loading position, the lugs 58, 58 are driven, in this embodiment upwards, towards the lower retaining element 44 of the loading unit 42 such as to move the lower retaining element 44 of the loading unit 42 relative to the upper retaining element 45 of the loading unit 42 which is constrained by the bottom end of the container 35 of the substance supply unit 31, and thereby load the loading unit 42.

The release mechanism 34 comprises a locking assembly 59 which acts to lock the substance supply unit 31 in the non-actuated position, in this embodiment by preventing movement of the pump fitting 36 relative to the outlet stem 37 of the substance supply unit 31, until actuation of the release mechanism 34, and a trigger member 61 which is coupled to the locking assembly 59 and disposed at the mouthpiece 19 such as to support the locking assembly 59 until acted upon by an oral exhalation breath of a user.

In this embodiment the locking assembly 59 comprises a body member 62 which is fixed to the outlet block 40 of the outlet unit 32, a first, support member 63, which is hinged, in this embodiment about a hinge axis 64 to the body member 62, and engages the pump fitting 36 of the substance supply unit 31 in the locked position, a second, link member 65 which is hinged about a hinge axis 66 to the support member 63 between a first, locking position and a second, release position, and couples the support member 63 to the trigger member 61 when loaded, a first biasing element 67, in this embodiment a resilient element, here a tension spring, which is coupled to the body member 62 and the support member 63 such as to bias the support member 63 to the locking position, and a second biasing element 69, in this embodiment a resilient element, here compression springs, which is coupled to the support member 63 and the link member 65 such as to bias the link member 65 to the locking position.

In this embodiment the body member 62 includes a support member stop 70 which defines the locking position of the support member 63 where the support member 63 is biased to the locking position.

In this embodiment the hinge axis 64 of the support member 63 is offset from the longitudinal axis of the substance supply unit 31, such that, on release of the link member 65 from the locking position, the support member 63 is hinged upwardly by the action of the substance supply unit 31 being driven upwardly by the loading unit 42.

In this embodiment the support member 63 comprises first and second arms 73, 75 which extend in opposite directions and define an abutment surface 77 at the junction therebetween, and, with the support member 63 in the locking position, the abutment surface 77 engages the upper end of the pump fitting 36 of the substance supply unit 31, the first arm 73 extends over the upper end of the pump fitting 36 in a direction substantially orthogonal to the longitudinal axis of the substance supply unit 31 and the second arm 75 is inclined upwardly such as to engage the support member stop 70 on the body member 62.

In this embodiment the first arm 73 of the support member 63 includes a first link member stop 79 against which the link member 65 is biased in the locking position, with

the first link member stop 79 being configured such that the link member 65 extends substantially orthogonally to the first arm 73 of the support member 63, and parallel to the longitudinal axis of the substance supply unit 31, when in the locking position.

In this embodiment the first arm 73 of the support member 63 includes a second link member stop 81 which acts to limit the rotation of the link member 65 when released from the locking position.

In this embodiment the link member 65 is a substantially rigid member which includes at least one, in this embodiment first and second engagement elements 83, 83 which engage the trigger member 61 when the link member 65 is in the locking position. In this embodiment the engagement elements 83, 83 each include an end cap 85 which is formed of a material of a high coefficient of friction, such as a rubber material, to provide for controlled engagement with the trigger member 61, and thereby prevent uncontrolled slipping from the trigger member 61. In an alternative embodiment the link member 65 could comprise a flexible, preferably resilient, element.

In this embodiment the trigger member 61 comprises a pivot pin 87 about which the trigger member 61 is rotatable between a first, supporting position in which the trigger member 61 engages the link member 65 in the locked position, and a second, released position in which the link member 65 is not supported, in having been caused to roll off the pivot pin 87, and released from the locking position.

In this embodiment the trigger member 61 further comprises a flow-sensitive vane 89 which extends from the pivot pin 87 and substantially closes the main flow path 21 when in the supporting position. In this embodiment the vane 89 is configured to engage the vane stop 29 on the arcuate section 27 of the guide member 20 when in the supporting position. In this embodiment the vane 89 includes an aperture 90 which acts to require a predetermined air flow through the main flow path 21 prior to releasing the trigger member 61 from the supporting position. Advantageously, with this configuration, a bi-directional air flow can be achieved through the nasal cavities prior to release of substance through the nosepiece 17. In an alternative embodiment, an air flow can be provided through the main flow path 21 prior to releasing the trigger member 61

from the supporting position by sizing the vane 89 to be of a size slightly smaller than the section of the main flow path 21, whereby an air flow of up to a predetermined flow rate can be developed about the vane 89 prior to driving the vane 89 such as to cause the trigger member 61 to be released from the supporting position.

The delivery device further comprises a pressure-sensitive sealing unit 93 which is configured normally to be closed, and thereby isolate the gas venting path 26 from the main flow path 21, such that the exhaled air flow of a user is directed through the main flow path 21, and be opened where the pressure in the main flow path 21 exceeds a predetermined threshold pressure such that an air flow can be developed over the vane 89 of the trigger member 61 which has a sufficient flow rate as to drive the vane 89 to actuate the locking assembly 59, with the exhaled air flow being vented through the external venting apertures 25, 25. As mentioned hereinabove, this configuration enables actuation of the release mechanism 34 in the event that the nasal passage of the user is so congested as to prevent the attainment of a sufficient flow rate as to drive the vane 89 of the trigger member 61 to actuate the release mechanism 34.

In this embodiment the sealing unit 93 comprises an annular seal 95 which is disposed such as to be a sealing fit at one, the upstream, end of the gas venting path 26, a sealing member 97 which is moveable between a first, normally closed position and a second, open position, and a biasing element 99, in this embodiment a resilient element, here a compression spring, for biasing the sealing member 97 to the closed position. The sealing member 97 includes an annular seat 101 and is movable between the closed position in which the annular seat 101 is in sealing engagement with the annular seal 95, with the annular seat 101 being maintained in sealing engagement with the annular seal 95 by the biasing element 99, and thereby closes the sealing unit 93 to isolate the gas venting path 26 from the main flow path 21, and the open position in which the sealing member 97 is driven out of sealing engagement with the annular seal 95 by the generation of a predetermined venting pressure in the main flow path 21, with the force generated by the venting pressure exceeding the biasing force applied by the biasing element 99, and thereby providing for fluid communication between the main flow path 21 and the gas venting path 26 such as to enable an air flow to be developed over the vane 89 of the trigger member 61 as required to actuate the release mechanism 34.

Operation of the delivery device will now be described hereinbelow.

In operation, a user first takes the device, as illustrated in Figure 7(a), and primes the device by rotating the loading member 51 of the loading mechanism 33 to the loaded position, as illustrated in Figure 7(b). With the release mechanism 34 in the locked configuration, that is, with the abutment surface 77 of the supporting member 73 of the locking assembly 59 abutting the pump fitting 36, the loading unit 42 is biased against the bottom of the container 35 of the substance supply unit 31. The user then inserts the nosepiece 17 into one of the nasal cavities, grips the mouthpiece 19 with the lips, and exhales through the mouthpiece 19. Where an air flow can be established through the main flow path 21, by virtue of the aperture 90 in the vane 89 of the trigger member 61, a bi-directional air flow is developed through the nasal cavities. As illustrated in Figure 7(c), with continued exhalation, the pressure differential across the vane 89 of the trigger member 61 increases, until such point that the pressure differential is such as to cause the rotation of the vane 89 and thereby the pivot pin 87 to which the vane 89 is attached. As illustrated in Figure 7(d), where an air flow cannot be established through the nosepiece 17, for example, as a result of nasal congestion, the pressure in the main flow path 21 increases, until such point that the pressure acts to open the sealing unit 93, in this embodiment by driving the sealing member 97 from the annular seal 95, at which point an air flow is established via the gas venting path 26 and the external venting apertures 25, 25 to atmosphere, which air flow is such as to cause the rotation of the vane 89 and thereby the pivot pin 87 to which the vane 89 is attached. This rotation of the pivot pin 87 is such as to cause the movement of the link member 65 of the locking assembly 59, which link member 65, once no longer abutting the pivot pin 87 and supporting the locking assembly 59 in the locking configuration, allows for the movement, under the action of the loading unit 42, of the container 35 and the pump fitting 36 coupled thereto to actuate the substance supply unit 31 and deliver a metered volume of liquid from the delivery tube 41 of the outlet unit 32.

Figures 8 and 9 illustrate a breath-actuated nasal delivery device in accordance with a second embodiment of the present invention.

The delivery device comprises a housing unit 114 which comprises a main body 115, a nosepiece 117 for fitting to a nostril of a user, and a mouthpiece 119 through which the user exhales to actuate the delivery device.

The main body 115 includes an aperture 116 for enabling any air flow thereinto to escape therefrom.

The main body 115 defines a main flow path 121 which provides a fluid communication path between the nosepiece 117 and the mouthpiece 119, and through which a substance is delivered to the nasal cavity of the user. The main flow path 121 includes an aperture 122 and an abutment 123 therein, the purpose of which will become apparent hereinbelow. In this embodiment the main flow path 121, in fluidly communicating the nosepiece 117 to the mouthpiece 119, is such that an exhalation breath of the user can provide for bi-directional flow through the nasal cavities as disclosed in WO-A-00/51672. In alternative embodiments there could be no fluid communication path between the nosepiece 117 and the mouthpiece 119 such that an exhalation breath of the user is not directed to the nasal cavities of the user. These alternative embodiments include those where substance is delivered in a separate gas flow, such as from a pressurized canister, for example, a pMDI canister.

In this embodiment the nosepiece 117 has a tapering section which narrows to the distal end thereof and acts, when inserted, typically from about 1 to 2 cm, into the anterior part of a nasal cavity, to expand the narrow nasal valve of the nasal cavity and provide a fluid-tight seal.

In this embodiment the mouthpiece 119 is configured to be gripped in the lips of a user. In an alternative embodiment the mouthpiece 119 could be configured to be gripped by the teeth of a user and sealed by the lips of the user. In a preferred embodiment the mouthpiece 119 is specifically configured to have one or both of a shape and geometry which allows the delivery device to be gripped repeatedly in the same position, thereby providing for the nosepiece 117 to be reliably inserted in the same position in the nasal cavity.

The delivery device further comprises a breath-actuated substance delivery assembly 124 for delivering substance through the main flow path 121 on exhalation by the user through the mouthpiece 119.

The substance supply assembly 124 comprises a substance supply unit 125 for delivering a metered dose of a substance on actuation of the same, an outlet unit 127 which is connected to the substance supply unit 125 for delivering substance through the main flow path 121, a loading mechanism 129 for loading the substance supply unit 125, and a release mechanism 131 for releasing the substance supply unit 125 from a loaded, non-actuated position to the actuated position on exhalation by the user through the mouthpiece 119.

In this embodiment the substance supply unit 125, as a mechanical pump, comprises a container 133 containing a volume of liquid containing a substance, a pump fitting 135 which includes a metering chamber and is connected to the container 133, and an outlet stem 137 which is movably disposed to the pump fitting 135 and through which liquid is delivered. In operation, a metered volume of liquid is delivered on relative movement of the pump fitting 135 and the outlet stem 137, in this embodiment movement of the pump fitting 135 in relation to the outlet stem 137, between a first position, as illustrated in Figure 8(a), in which the outlet stem 137 is extended from the pump fitting 135 and a second position, as illustrated in Figure 8(c), in which the outlet stem 137 is depressed into the pump fitting 135.

In this embodiment the substance supply unit 125 is a multi-dose device for enabling the delivery of a succession of metered doses of substance. In an alternative embodiment the substance supply unit 125 could be a single dose device for delivering a single metered dose of substance.

The pump fitting 135 includes at least one lug 138 which provides an abutment surface 139, as will be described in more detail hereinbelow. In this embodiment the abutment surface 139 of the at least one lug 138 is an inclined surface.

The outlet unit 127 comprises an outlet block 140 which is connected to the outlet stem 137 of the substance supply unit 125 and, in this embodiment, includes a valve and swirl chamber, and a delivery tube 141 from which a mist of fine droplets of the liquid is expelled on actuation of the substance supply unit 125. In an alternative embodiment the delivery tube 141 could be configured to deliver a liquid jet.

The loading mechanism 129 comprises a biasing element 143, in this embodiment a resilient element, here a compression spring, which is loaded with a predetermined force which is sufficient to actuate the substance supply unit 125 when released, in this embodiment by causing relative movement of the pump fitting 135 in relation to the outlet stem 137, and a loading member 145 for loading the biasing element 143. In this embodiment the loading member 145 comprises a lever which is movable to a loading position, as illustrated in Figure 8(b), in which the loading member 145 acts to load the biasing element 143 by biasing the same against the bottom end of the container 133 of the substance supply unit 125.

The release mechanism 131 comprises a locking assembly 147 which acts to lock the substance supply unit 125 in the non-actuated position, in this embodiment by preventing movement of the pump fitting 135 relative to the outlet stem 137, until actuation of the release mechanism 131, and a trigger member 149 which is coupled to the locking assembly 147 and disposed at the mouthpiece 119 such as to support the locking assembly 147 until acted upon by an oral exhalation breath of a user.

In this embodiment the locking assembly 147 comprises a first, support member 151, which is hinged, in this embodiment to the outlet block 140 of the outlet unit 127, and engages the at least one lug 138 on the pump fitting 135 in the locked position, and a second, link member 153 which couples the support member 151 to the trigger member 149 when loaded.

In this embodiment the support member 151 is substantially L-shaped, with one end thereof being hinged to the outlet block 140 of the outlet unit 127, the other end thereof supporting the link member 153, and including an abutment surface 155, in this embodiment a curved surface, which engages the abutment surface 139 of the at least

one lug 138 in the locked position. In this embodiment the link member 153 is hinged to the support member 151 such as to be freely movable between a first, locked position, as illustrated in Figure 8(a), in which the link member 153 abuts the support member 151 and defines a support position, and a second, released position. In an alternative embodiment the link member 153 could comprise a flexible, preferably resilient, element.

In this embodiment the trigger member 149 comprises a pivot pin 157 about which the trigger member 149 is rotatable between a first, supporting position, as illustrated in Figure 8(a), in which the trigger member 149 engages the locking assembly 147 in the locked position, and a second, released position, as illustrated in Figure 8(c), in which the locking assembly 147 is not supported and released from the locking position.

In this embodiment the trigger member 149 further comprises a first, flow-sensitive vane 159 which extends from the pivot pin 157 and substantially closes the main flow path 121 when in the supporting position. In this embodiment the first vane 159 is configured to engage the abutment 123 in the main flow path 121 when in the supporting position. The provision of the abutment 123 acts to prevent the actuation of the substance supply unit 125 on inhalation by the user. In this embodiment the first vane 159 includes an aperture 160 which acts to require a predetermined air flow through the main flow path 121 prior to releasing the trigger member 149 from the supporting position. Advantageously, with this configuration, a bi-directional air flow can be achieved through the nasal cavities prior to release of substance through the nosepiece 117.

In this embodiment the trigger member 149 further comprises a second, pressure-sensitive vane 161 which extends from the pivot pin 157 and substantially seals the aperture 122 in the main flow path 121 when in the supporting position. In this embodiment the second vane 161 is configured such as to release the trigger member 149 from the supporting position on the generation of a predetermined pressure in the main flow path 121. Advantageously, with this configuration, the substance supply unit 125 can be actuated even when the nasal cavity is so congested that no, or not sufficient, an air flow can be achieved.

Operation of the delivery device will now be described hereinbelow.

In operation, a user first primes the device by rotating the loading member 145 of the loading mechanism 129 to the loaded configuration, as illustrated in Figure 8(b). With the release mechanism 131 in the locked position, that is, with the abutment surface 155 of the supporting member 151 of the locking assembly 147 abutting the abutment surface 139 of the at least one lug 138 on the pump fitting 135, the biasing element 143 is biased against the bottom of the container 133 of the substance supply unit 125. The user then inserts the nosepiece 117 into one of the nasal cavities, grips the mouthpiece 119 with the lips, and exhales through the mouthpiece 119. Where an air flow can be established through the main flow path 121, by virtue of the aperture 160 in the first vane 159 of the trigger member 149, a bi-directional air flow is developed through the nasal cavities. With continued exhalation, the pressure differential across the first vane 159 of the trigger member 149 increases, until such point that the pressure differential is such as to cause the rotation of the first vane 159 and thereby the pivot pin 157 to which the first vane 159 is attached. Where an air flow cannot be established, for example, as a result of nasal congestion, the pressure in the main flow path 121 increases, until such point that the pressure acts to cause the rotation of the second vane 161 and thereby the pivot pin 157 to which the second vane 161 is attached. This rotation of the pivot pin 157 is such as to cause the movement of the link member 153 of the locking assembly 147, which link member 153, once no longer abutting the pivot pin 157 and supporting the locking assembly 147 in the locking configuration, allows for the movement, under the action of the biasing element 143, of the container 133 and the pump fitting 135 coupled thereto to actuate the substance supply unit 125 and deliver a metered volume of liquid from the delivery tube 141 of the outlet unit 127.

Figures 10 and 11 illustrate a breath-actuated nasal delivery device in accordance with a third embodiment of the present invention.

The nasal delivery device of this embodiment is very similar to that of the above-described second embodiment. Thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like parts being designated by like reference signs.

The nasal delivery device of this embodiment differs only in that the trigger member 149 does not include a second vane 161 as in the above-described second embodiment, but instead comprises a resilient element 163 which acts as a pressure-sensitive element. Operation is the same as for the above-described embodiment, with the resilient element 163 being deformed, and hence causing rotation of the pivot pin 157, with an increased pressure in the main flow path 121, such that the pivot pin 157 is rotated sufficiently to release the locking assembly 147 on a predetermined pressure being developed in the main flow path 121.

In alternative embodiments the trigger member 149 could be configured to include only a single vane 159, 161 or element 163 such that the trigger member 149 is only one of flow or pressure sensitive. In particular, where the exhalation breath of a user is not delivered to the nasal airway, that is, where the nosepiece 117 is not fluidly connected to the mouthpiece 119, the trigger member 149 need only be configured to be one of flow or pressure sensitive, since there will be no obstruction to the exhalation breath.

For example, in these embodiments the substance supply unit 125 could comprise an aerosol canister, such as used in a pressurized metered dose inhaler (pMDI), for delivering a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing a substance, preferably a medicament either as a suspension or a solution.

In other embodiments the substance supply unit 125 could comprise a dry powder delivery unit for delivering a metered dose of substance in a dry powder, either entrained in the exhalation breath of a user or in a separate gas flow as supplied by a separate gas source.

In still yet other embodiments the substance supply unit 125 could comprise a nebulizer for delivering a metered dose of a nebulized substance, either entrained in the exhalation breath of a user or in a separate gas flow as supplied by a separate gas source.

In still yet also other embodiments the substance supply unit 125 could comprise a jet pump which delivers, in this embodiment squirts, a metered dose of a substance as a jet on actuation thereof, typically by releasing the stored energy in a compression spring.

In these embodiments the delivery device is configured to deliver the exhalation breath through one nostril of a user such as to flow around the posterior margin of the nasal septum and out of the other nostril of the user, thereby achieving bi-directional flow through the nasal cavities as disclosed in WO-A-00/51672.

In alternative embodiments the delivery device could be configured to deliver substance at a reduced pressure which is not sufficient to achieve bi-directional delivery through the nasal cavities. This notwithstanding, these embodiments are still advantageous as compared to known delivery devices in providing for velum closure and being capable of achieving targeted delivery. In one embodiment the delivery device could include two nosepieces 117 for the simultaneous delivery to each of the nasal cavities. This embodiment advantageously provides for three-point fixation of the delivery device via the nosepieces 117 and the mouthpiece 119.

Figures 12 and 13 illustrate a breath-actuated nasal delivery device in accordance with a fourth embodiment of the present invention.

The nasal delivery device of this embodiment is very similar to that of the above-described second and third embodiments. Thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like parts being designated by like reference signs.

The nasal delivery device of this embodiment differs principally only in that the substance supply unit 125 is an aerosol canister, such as used in a pressurized metered dose inhaler (pMDI), for delivering a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing a substance, in that the release mechanism 131 further comprises a biasing element 169, in this embodiment a resilient element, for biasing the locking assembly 147 to the locking configuration, and in that the trigger member 149 comprises only a single flow-sensitive vane 159. In a preferred embodiment the aerosol

canister is a pressurized metered dose inhaler (pMDI), for delivering a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing a substance, preferably a medicament either as a suspension or a solution. Operation is the same as for the above-described second and third embodiments.

Figures 14 and 15 illustrate a flow-control mechanism in accordance with an embodiment of the present invention for incorporation in the main flow path 21, 121 between the mouthpiece 19, 119 and the trigger member 61, 149 of the nasal delivery devices of the above-described embodiments.

Where a spray pump is operated in an inclined orient, typically more than 45 degrees, or an upside-down orient, air may be drawn into the pump fitting, causing at least in part air, and not liquid, to be pumped. This will have the effect of causing a sequence of subsequent doses to be incomplete, and the flow-control mechanism is configured thus to prevent a user from releasing the device in an incorrect orient.

In this embodiment, as illustrated in Figure 14(a), the flow-control mechanism comprises a flow channel section 171 which includes a recess 173, and a ball 175 which is movably captively disposed within the flow channel section 171 and normally, with the delivery device in an acceptable orient, rests in the recess 173 to allow an air flow from the mouthpiece 19, 119 to the trigger member 61, 149, but, with the delivery device in an unacceptable orient, the ball 175 adopts a forward, downstream position in the flow channel section 171 to block the same and prevent the development of an air flow therethrough which is required to actuate the release mechanism 34, 131. A user is most likely to attempt to operate the device when seated with their head tilted backwards or in the supine position. Where the device is tilted backwards more than a predetermined angle, as illustrated in Figure 14(b), the ball 175 will roll from the recess 173 into a narrower, downstream part of the flow channel section 171 and block the same, thereby preventing actuation of the release mechanism 34, 131. A more complex mechanism may also prevent insufflations in this position.

In this embodiment the flow-control mechanism is also configured to prevent actuation of the release mechanism 34, 131 where a user blows too forcefully into the device. It

can be advantageous to first establish a certain flow through the device and into the nose before releasing substance. The shape and/or geometry of the flow channel section 171 at the recess 173 allows for the passage of a certain air flow, as illustrated in Figure 15(a), but, if the air flow becomes too high, the ball 175 is blown into the narrow, downstream region of the flow channel section 175, as illustrated in Figure 15(b), blocking off the flow channel section 171, and hence the main flow path 21, 121, and thereby preventing air flow through the main flow path 21, 121, and consequently actuation of the device. The shape and geometry of the recess 173, the angling of the flow channel section 171 at the end regions thereof and the weight of the ball 175 can be altered to determine the maximum permitted flow.

Also, in this embodiment, where inhalation is attempted, the ball 175 will be sucked into the narrow, upstream region of the flow channel section 171, preventing further air flow, as illustrated in Figure 15(c).

Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined in the appended claims.

For example, for mechanical spray pumps, issues related to priming and loss of priming are important. Normally, when the container 35, 133 is new, the pump must be compressed typically three to five times before providing the first mist at actuation. In order to ensure that the required priming is performed before the device is used, in one modification a counter is included which clearly shows that the device is primed. The subject should be able to see that the device actually fires before it is used.

In another modification the device is configured to provide for manual firing, especially in the case where a conventional container 35, 133 is used which may suck air into the tube and chamber if the container 35, 133 is held in an incorrect orient. With the traditional spray pumps, the dose in the chamber tends to evaporate after some hours or days, making it necessary to re-prime the pump to enable proper function where having not been used for a certain period. However, recently, a new pump design has been developed which incorporates a valve, preventing this loss of prime. Still, the problem

of actuating in an upside-down or very-tilted position remains. If actuated in this position, air may be drawn into the tube inside the container 35, 133 instead of liquid. This causes one or more of the subsequent doses to be incomplete. This may require repeated re-priming to restore normal function. One solution is to provide a compliant membrane inside the container 35, 133 to prevent air entering the tube. Still, this solution is more expensive and the flexible membrane inside the container 35, 133 is formed other than from glass. To change from glass may be costly, and may hinder the uptake of this solution, particularly where used for medicaments. The present mechanism, which prevents release in upside-down and very-tilted orients, will to a large extent obviate this problem.

In the described embodiments the hinge axis of the support member 63, 151 of the locking assembly 59, 147 is co-incident with the axis of the substance supply unit 31, 125, but the hinge axis of the support member 63, 151 could be offset from the axis of the substance supply unit 31, 125.

CLAIMS

1. A breath-actuated nasal delivery device, comprising:
a mouthpiece through which a user in use exhales to actuate the delivery device;
a nosepiece for fitting to a nostril of the user through which a substance is in use delivered;
a substance supply unit actuatable to deliver a dose of a substance through the nosepiece;
a loading unit operable to load the substance supply unit with an actuation force; and
a release mechanism for enabling actuation of the substance supply unit in response to exhalation by the user through the mouthpiece;
wherein the release mechanism comprises a locking unit which is movable between a locking configuration in which the substance supply unit is locked in a non-actuated position when loaded by the loading unit and a release configuration in which the substance supply unit is actuatable by the loading unit, and a trigger member for releasing the locking unit from the locking configuration to the release configuration in response to exhalation by the user through the mouthpiece and thereby enabling actuation of the substance supply unit.

2. The delivery device of claim 1, wherein the trigger member comprises a flow-sensitive element in fluid communication with the mouthpiece.

3. The delivery device of claim 2, wherein the flow-sensitive element comprises a vane.

4. The delivery device of claim 2 or 3, wherein the flow-sensitive element includes an aperture which allows for a predeterminable air flow thereover prior to actuation.

5. The delivery device of claim 2 or 3, wherein the flow-sensitive element is one or both of shaped and sized such as to allow for a predeterminable air flow thereover prior to actuation.

6. The delivery device of any of claims 1 to 5, wherein the trigger member comprises a pressure-sensitive element in fluid communication with the mouthpiece.

7. The delivery device of claim 6, wherein the pressure-sensitive element comprises a vane.

8. The delivery device of claim 6, wherein the pressure-sensitive element comprises a flexible membrane.

9. The delivery device of claim 8, wherein the flexible membrane comprises a resilient membrane.

10. The delivery device of claim 6, wherein the pressure-sensitive element comprises a flexible membrane in fluid communication with the mouthpiece and a vane operable by the flexible membrane.

11. The delivery device of claim 10, wherein the flexible membrane comprises a resilient membrane.

12. The delivery device of any of claims 1 to 5, further comprising:
a pressure-sensitive sealing unit disposed downstream of the trigger member and being operable to vent an air flow developed by the user on exhalation through the mouthpiece to atmosphere, the sealing unit being normally closed and operable such as to be opened on generation of a predeterminable pressure thereat.

13. The delivery device of claim 12, wherein the sealing unit comprises an annular seal, a sealing member movable between a closed position in sealing engagement

with the annular seal and an open position in which an air flow can flow through the annular seal, and a biasing element for normally biasing the sealing member to the closed position and enabling the sealing member to be opened on generation of a predeterminable pressure thereat.

14. The delivery device of claim 12, wherein the sealing unit comprises a flexible membrane which is movable between a closed position and an open position in which an air flow can flow thereby.

15. The delivery device of claim 14, wherein the flexible membrane comprises a resilient membrane.

16. The delivery device of any of claims 1 to 15, wherein the trigger member includes a pivot pin about which the same is rotatable, which pivot pin is engaged by the locking unit when in the locking configuration such that the locking unit is moved from the locking configuration to the release configuration on rotation of the pivot pin.

17. The delivery device of claim 16, wherein the locking unit includes a first, support member which abuts the substance supply unit in the locking configuration and a second, link member which engages the pivot pin of the trigger member in the locking configuration, wherein the link member is movable in relation to the support member and configured to be moved on rotation of the pivot pin to move the locking unit from the locking configuration to the release configuration.

18. The delivery device of claim 17, wherein the link member is rotatably connected to the support member.

19. The delivery device of claim 17 or 18, wherein the link member is configured to load the pivot pin radially.

20. The delivery device of any of claims 1 to 19, further comprising:

a flow path fluidly connecting the nosepiece and the mouthpiece, whereby an air flow developed by exhalation by the user through the mouthpiece is delivered through the nosepiece.

21. The delivery device of any of claims 1 to 19, wherein the nosepiece and the mouthpiece are fluidly isolated.

22. The delivery device of any of claims 1 to 21, wherein the substance supply unit comprises a nebulizer for supplying an aerosol.

23. The delivery device of any of claims 1 to 21, wherein the substance supply unit comprises an aerosol canister for supplying an aerosol.

24. The delivery device of any of claims 1 to 21, wherein the substance supply unit comprises a delivery pump unit for supplying one of an aerosol or a jet.

25. The delivery device of claim 24, wherein the delivery pump unit comprises a liquid pump unit for supplying a liquid aerosol.

26. The delivery device of claim 24, wherein the delivery pump unit comprises a powder pump unit for supplying a powder aerosol.

27. The delivery device of any of claims 1 to 21, wherein the substance supply unit comprises a powder delivery unit for delivering a powder aerosol.

28. The delivery device of any of claims 1 to 27, further comprising:
a flow-control mechanism disposed upstream of the trigger member to at least restrict an air flow to the trigger member such as to prevent actuation of the release mechanism on exhalation by the user through the mouthpiece where the delivery device is being improperly operated.

29. The delivery device of claim 28, wherein the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the delivery device is in an improper orient.

30. The delivery device of claim 28, wherein the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the air flow developed by the user has a rate exceeding a predeterminable threshold value.

31. The delivery device of any of claims 28 to 30, wherein the flow-control mechanism comprises a flow channel section which includes a recess, and a ball which is movably, captively disposed within the flow channel section, the ball normally, with proper operation of the delivery device, resting in the recess such as to allow a sufficient air flow to the trigger member as to enable actuation of the release mechanism, and being moved to at least partially block the flow channel section where the delivery device is being improperly operated such as to prevent actuation of the release mechanism.

32. A breath-actuated nasal delivery device, comprising:

a mouthpiece through which a user in use exhales to actuate the delivery device;

a nosepiece for fitting to a nostril of the user through which a substance is in use delivered and being in fluid communication with the mouthpiece;

a substance supply unit actuatable to deliver a dose of a substance through the nosepiece;

a release mechanism for enabling actuation of the substance supply unit in response to exhalation by the user through the mouthpiece; and

a flow-control mechanism disposed upstream of the trigger member to at least restrict an air flow to the trigger member such as to prevent actuation of the release mechanism on exhalation by the user through the mouthpiece where the delivery device is being improperly operated.

33. The delivery device of claim 32, wherein the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the delivery device is in an improper orient.

34. The delivery device of claim 32 or 33, wherein the flow-control mechanism is configured to at least restrict the air flow to the trigger member where the air flow developed by the user has a rate exceeding a predeterminable threshold value.

35. The delivery device of any of claims 32 to 34, wherein the flow-control mechanism comprises a flow channel section which includes a recess, and a ball which is movably, captively disposed within the flow channel section, the ball normally, with proper operation of the delivery device, resting in the recess such as to allow a sufficient air flow to the trigger member as to enable actuation of the release mechanism, and being moved to at least partially block the flow channel section where the delivery device is being improperly operated such as to prevent actuation of the release mechanism.

36. A release mechanism for enabling actuation of a substance supply unit, the release mechanism comprising:
a locking unit which is movable between a locking configuration in which the substance supply unit is locked in a non-actuated position and a release configuration in which the substance supply unit is actuatable; and
a trigger member for releasing the locking unit from the locking configuration to the release configuration in response to a gas flow thereat, wherein the trigger member includes a pivot pin about which the same is rotatable, which pivot pin is engaged by the locking unit when in the locking configuration such that the locking unit is moved from the locking configuration to the release configuration on rotation of the pivot pin.

37. The release mechanism of claim 36, wherein the locking unit includes a first, support member which abuts the substance supply unit in the locking configuration and a second, link member which engages the pivot pin of the

trigger member in the locking configuration, wherein the link member is movable in relation to the support member and configured to be moved on rotation of the pivot pin to move the locking unit from the locking configuration to the release configuration.

38. The release mechanism of claim 37, wherein the link member is rotatably connected to the support member.

39. The release mechanism of claim 37 or 38, wherein the link member is configured to load the pivot pin radially.

40. A breath-actuated nasal delivery pump for delivering a liquid containing a substance to a nasal cavity of a user.

41. The delivery pump of claim 40, wherein the delivery pump is a spray pump and the liquid is delivered as a liquid spray.

42. The delivery pump of claim 40, wherein the delivery pump is a jet pump and the liquid is delivered as a liquid jet.

43. A nasal delivery device substantially as hereinbefore described with reference to any of Figures 2 to 7, Figures 8 and 9, Figures 10 and 11 or Figures 12 and 13, optionally in conjunction with Figures 14 and 15, of the accompanying drawings.

44. A release mechanism substantially as hereinbefore described with reference to any of Figures 2 to 7, Figures 8 and 9, Figures 10 and 11 or Figures 12 and 13 of the accompanying drawings.

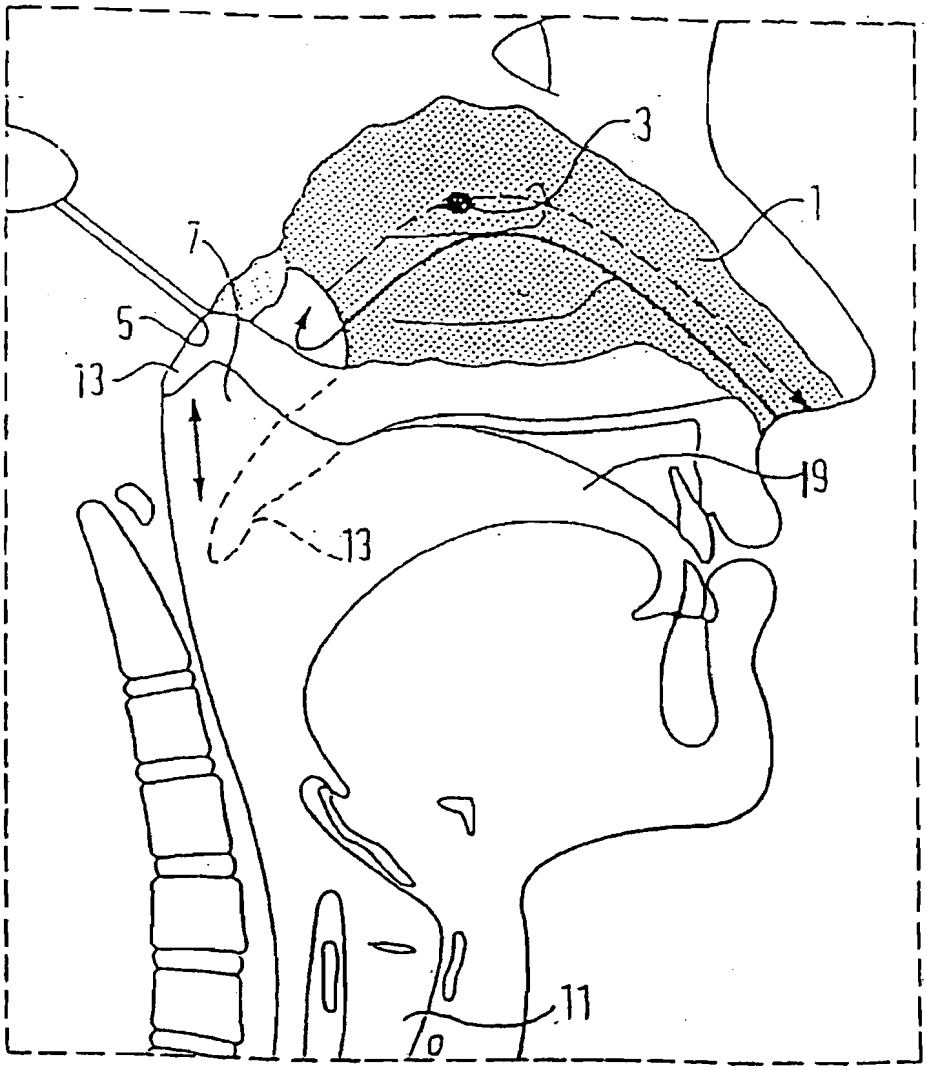


FIG. 1

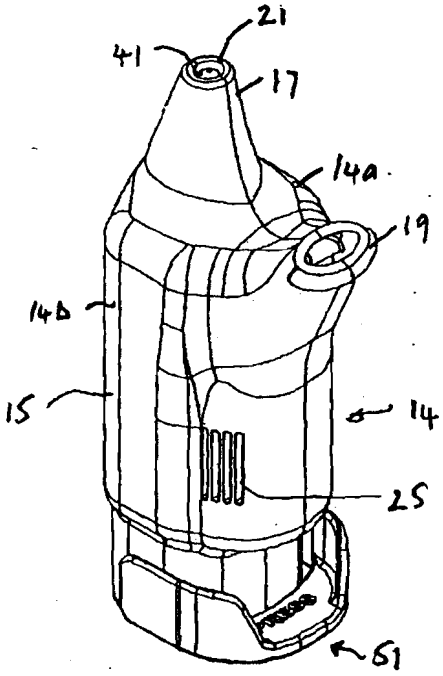


Fig. 2(a)

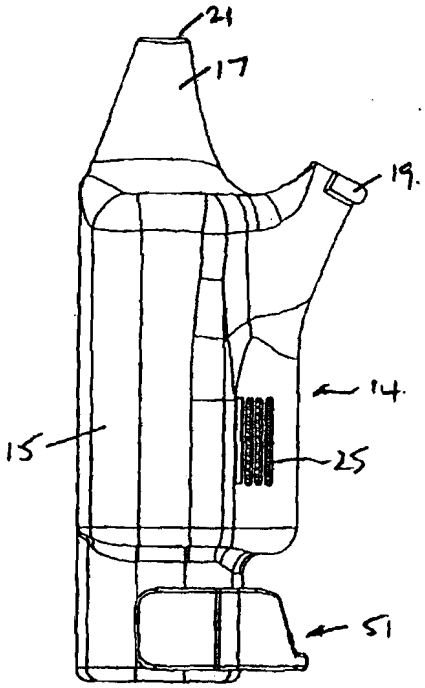


Fig. 2(b)

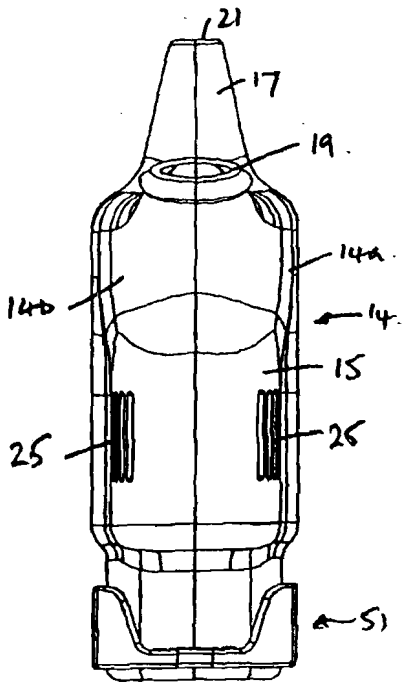


Fig. 2(c)

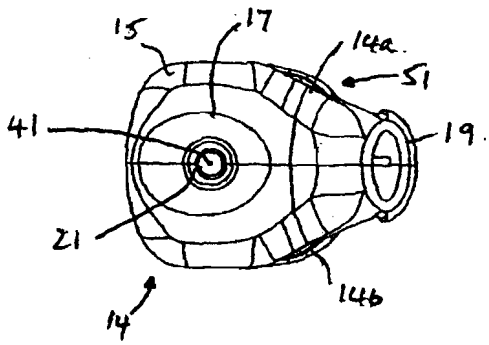


Fig. 2(d)

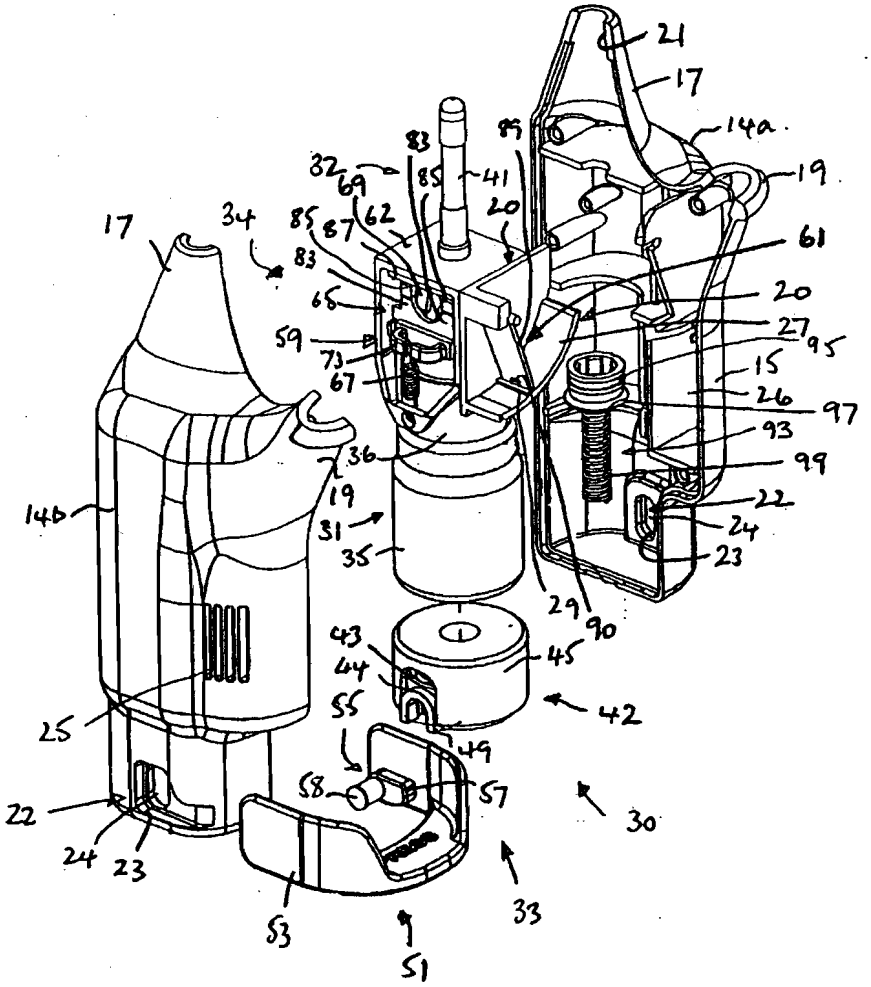

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Fig. 3

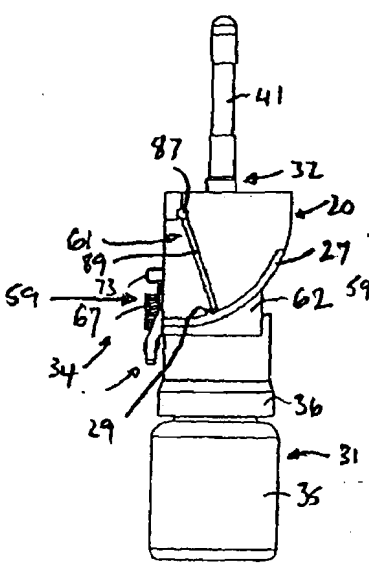


Fig. 4(a).

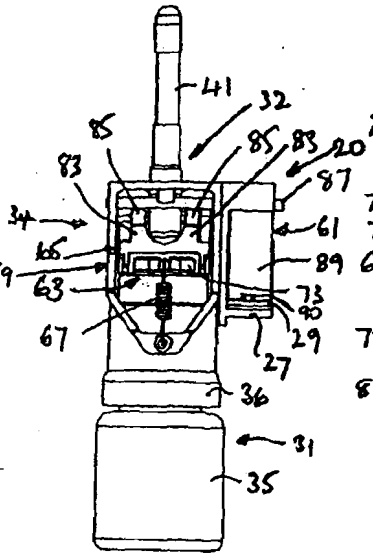


Fig. 4(b)

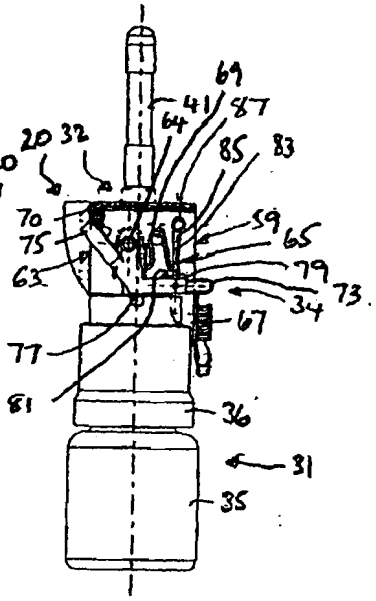


Fig. 4(c)

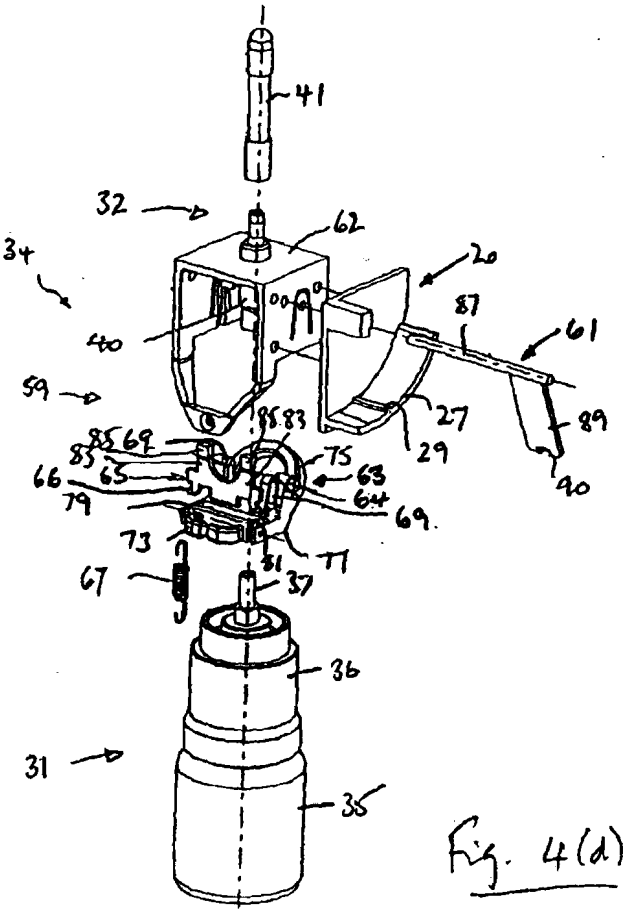


Fig. 4(d)

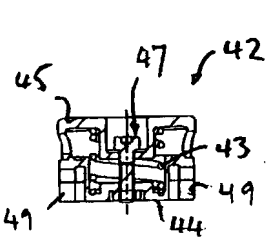


Fig. 5(b)

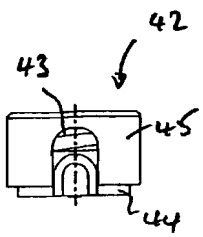


Fig. 5(a)

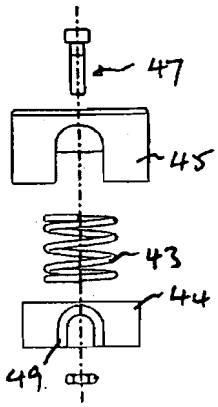


Fig. 5(c)

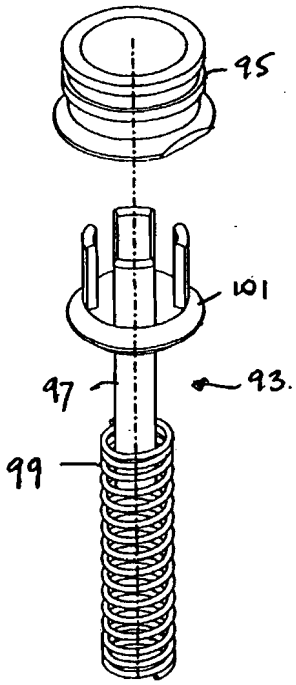


Fig. 6(d)

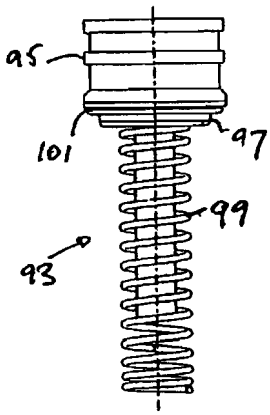
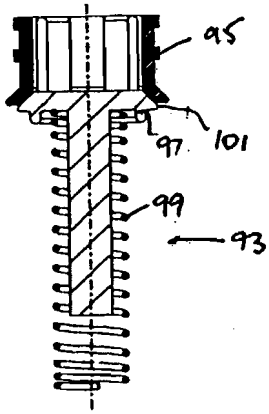


Fig. 6(a)



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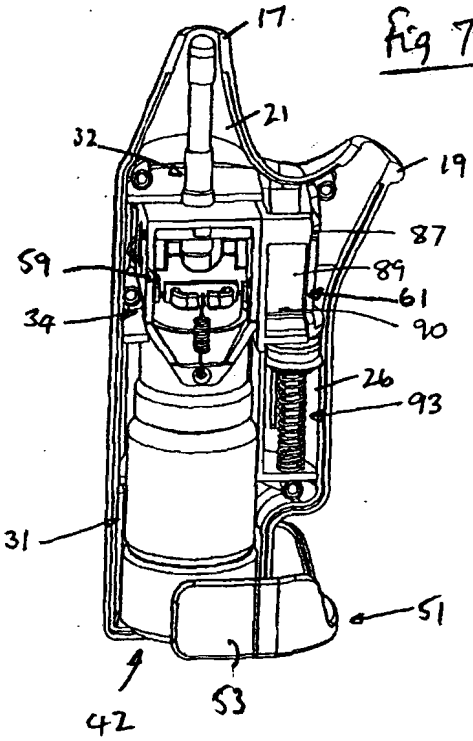
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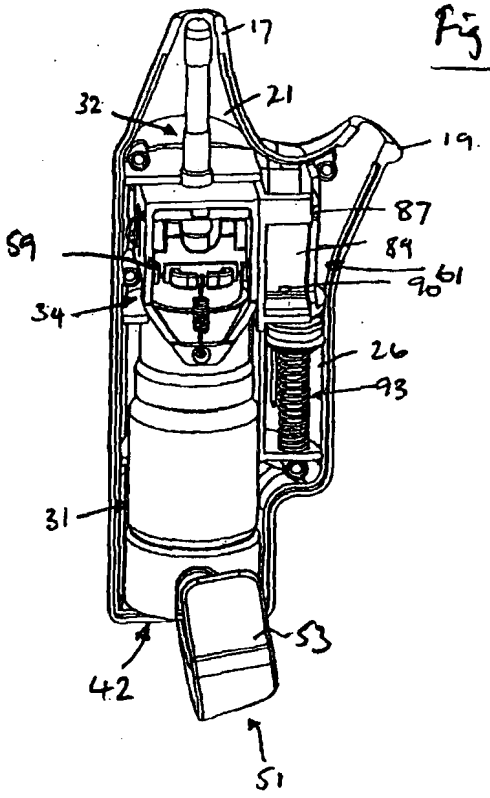
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Fig. 7(b)

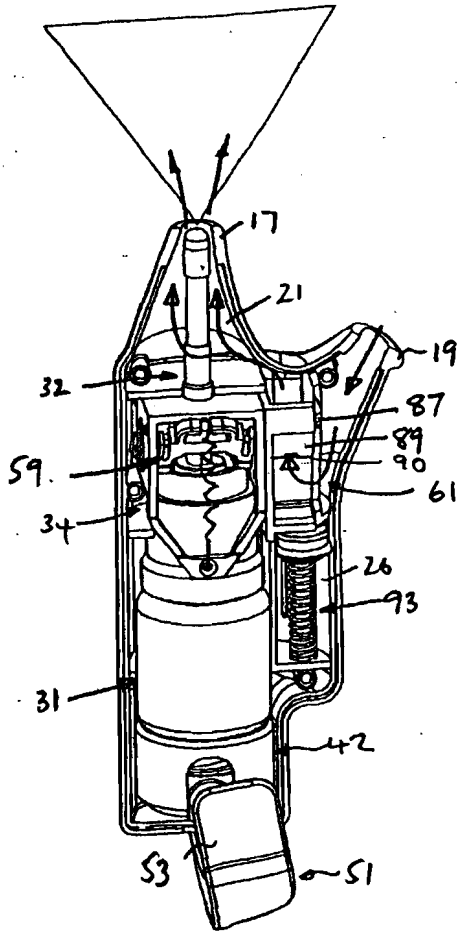
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Fig. 7(c)

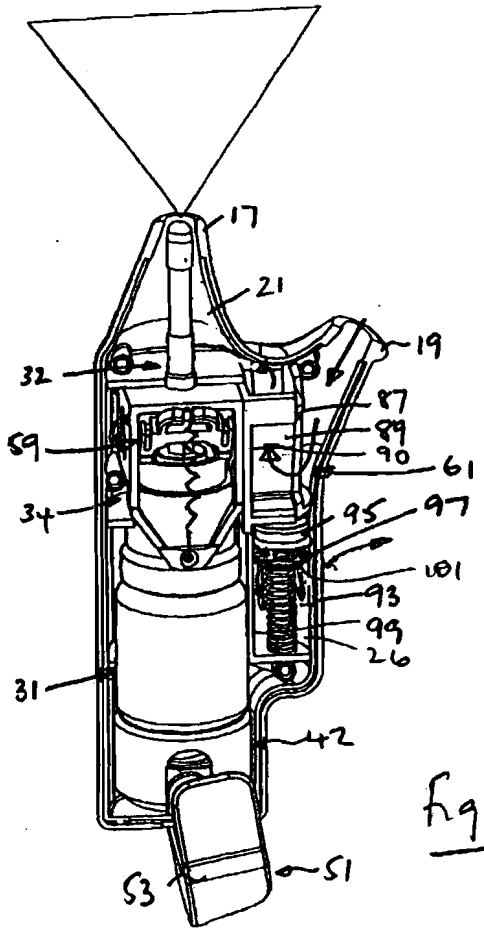
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Fig. 7(d)

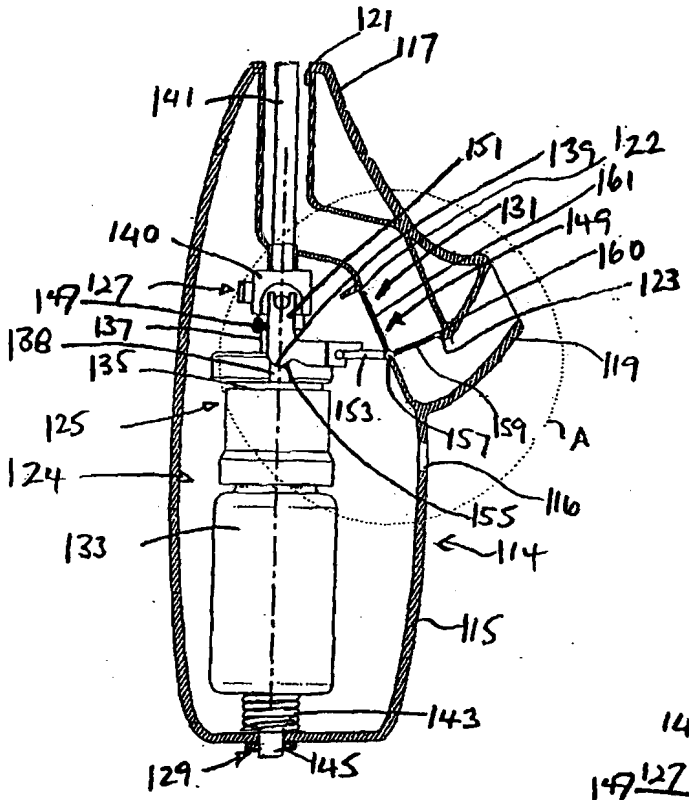
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Fig 8(a)

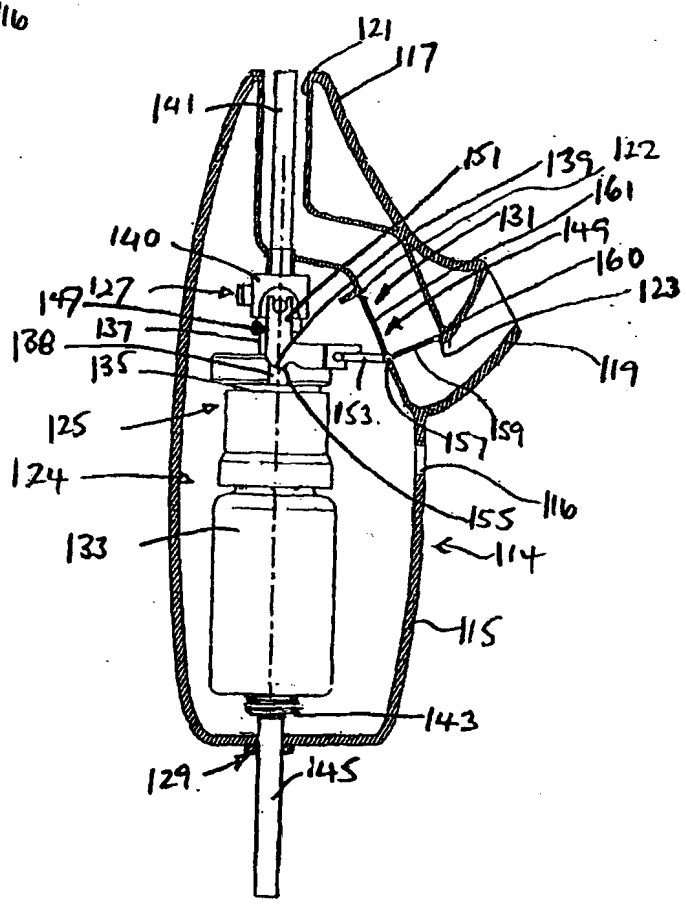
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Fig 8(b)

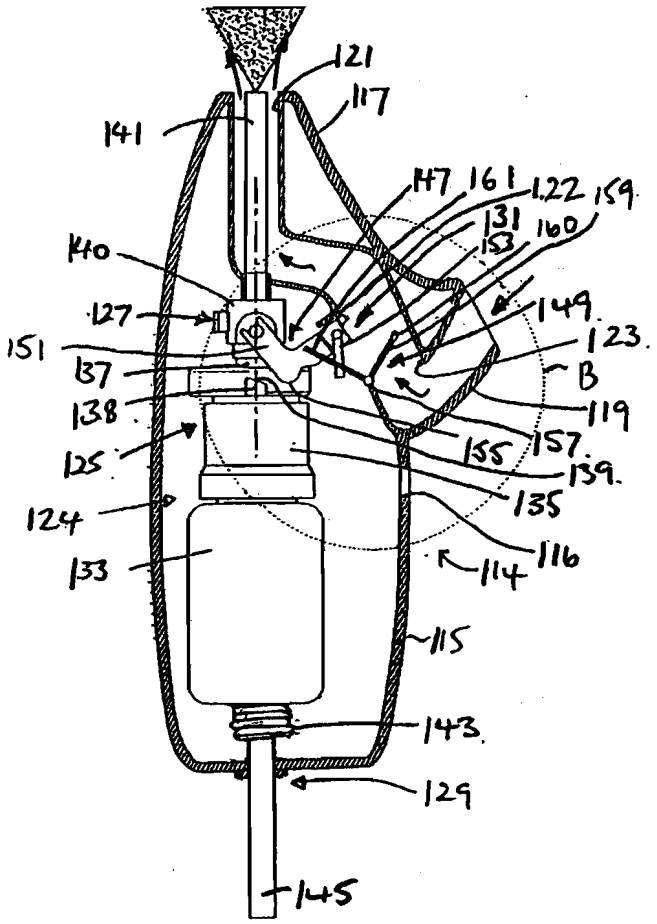
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Fig. 8(c)

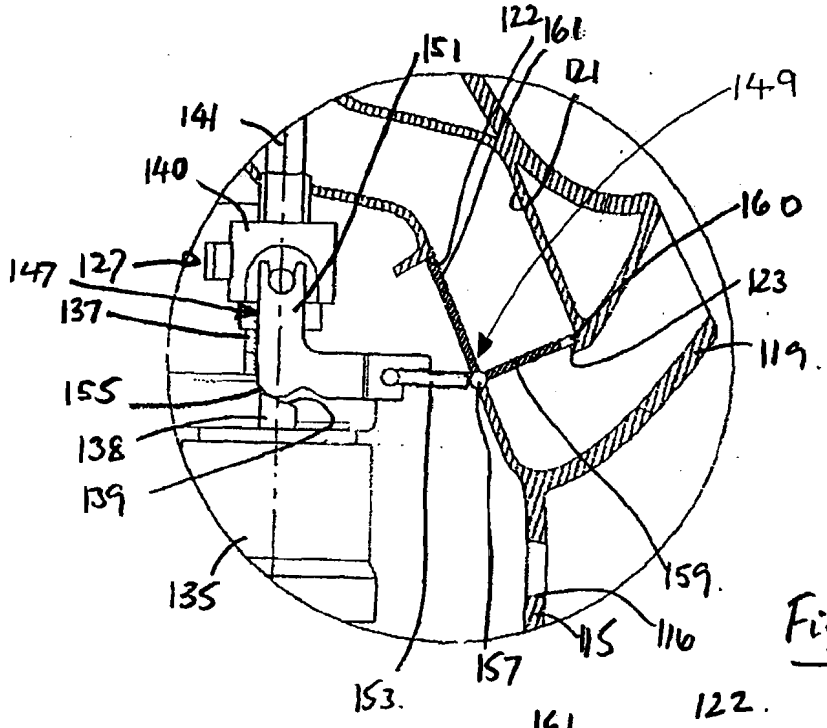
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Fig. 9(a)

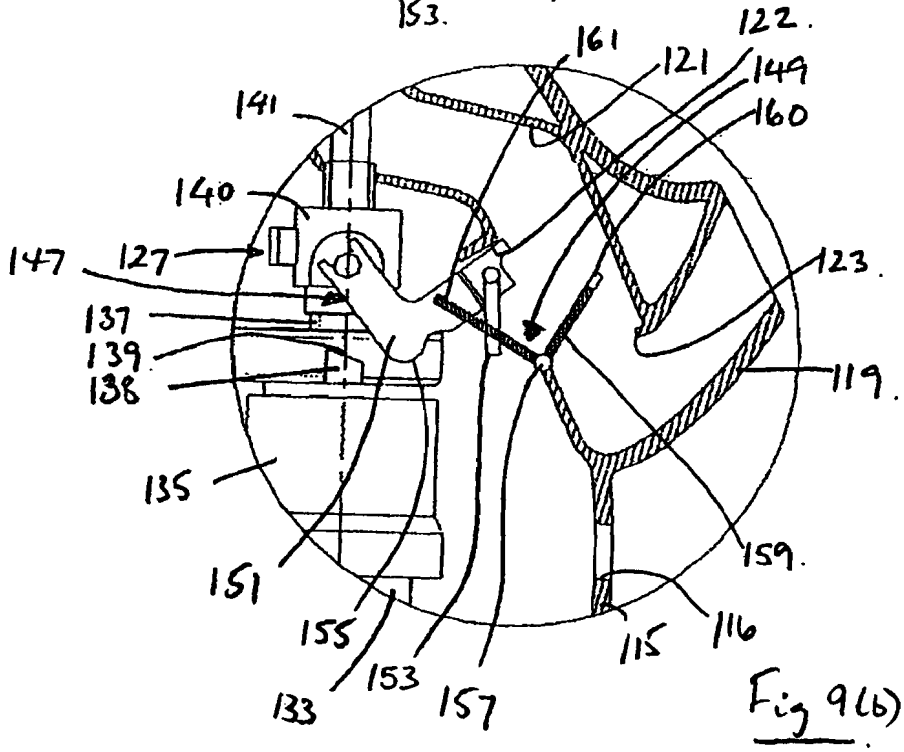
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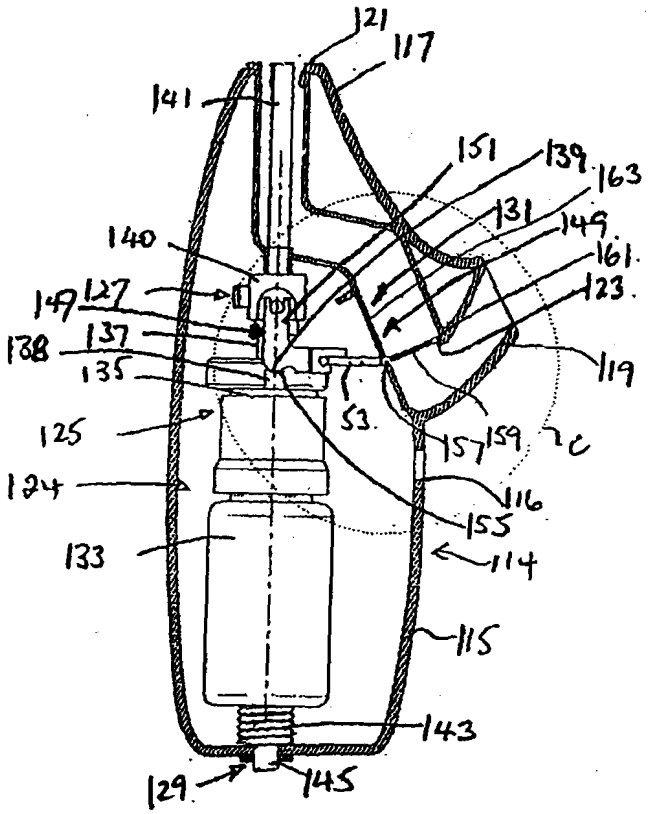
Fig 9(b)



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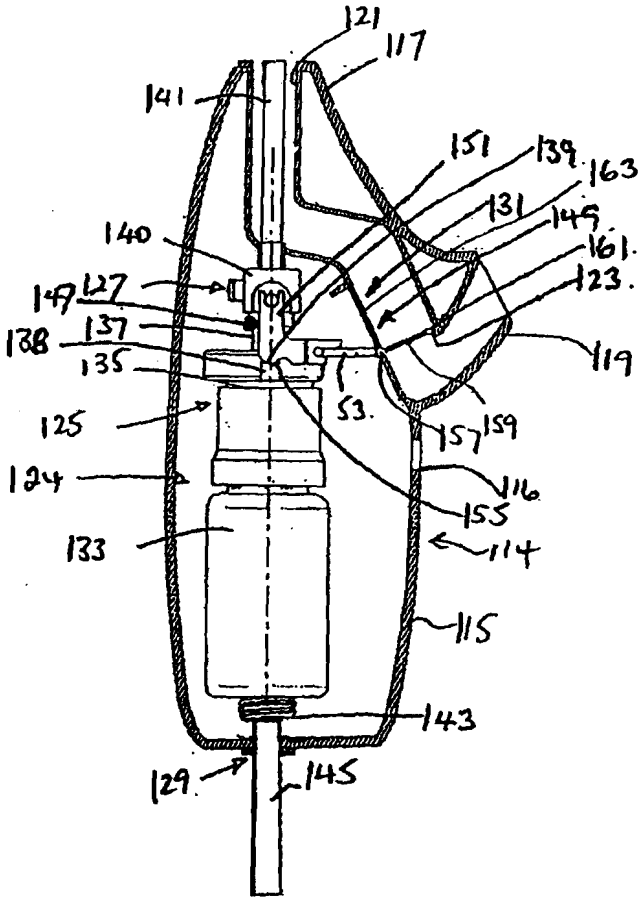

Fig. 10(b)

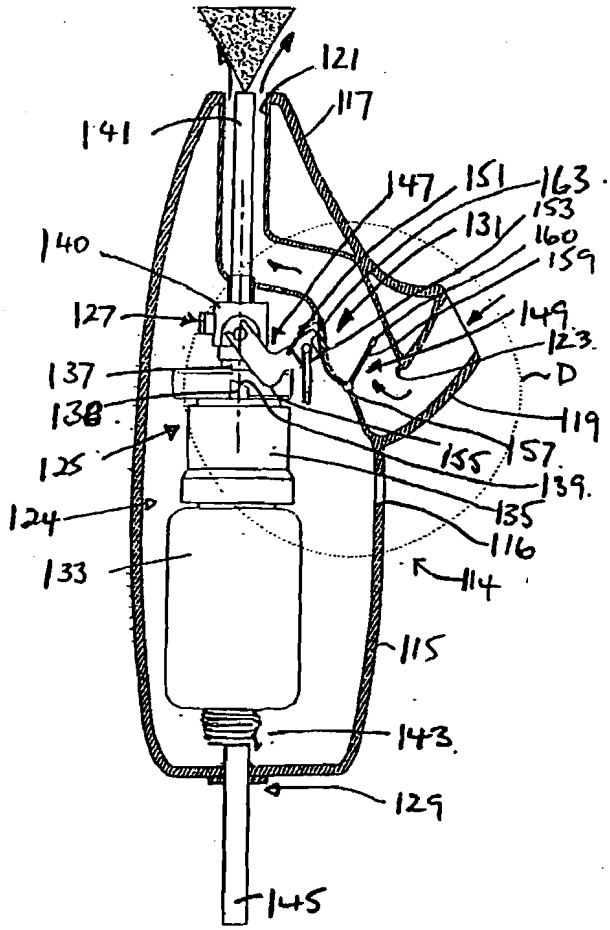
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Fig. 10(c)

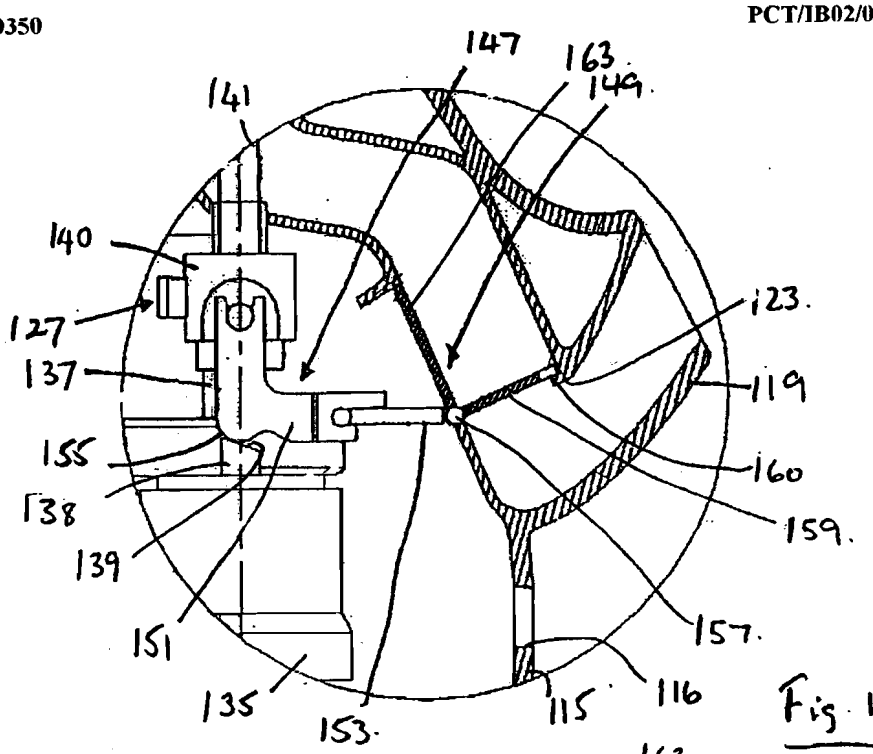

Fig 11(a)

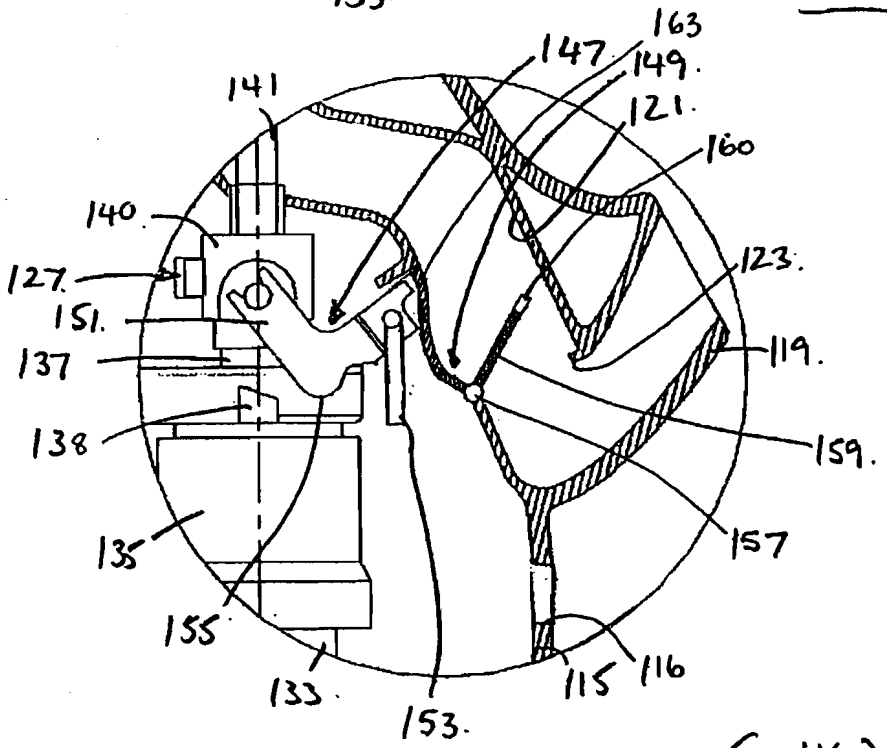

Fig 11(b)

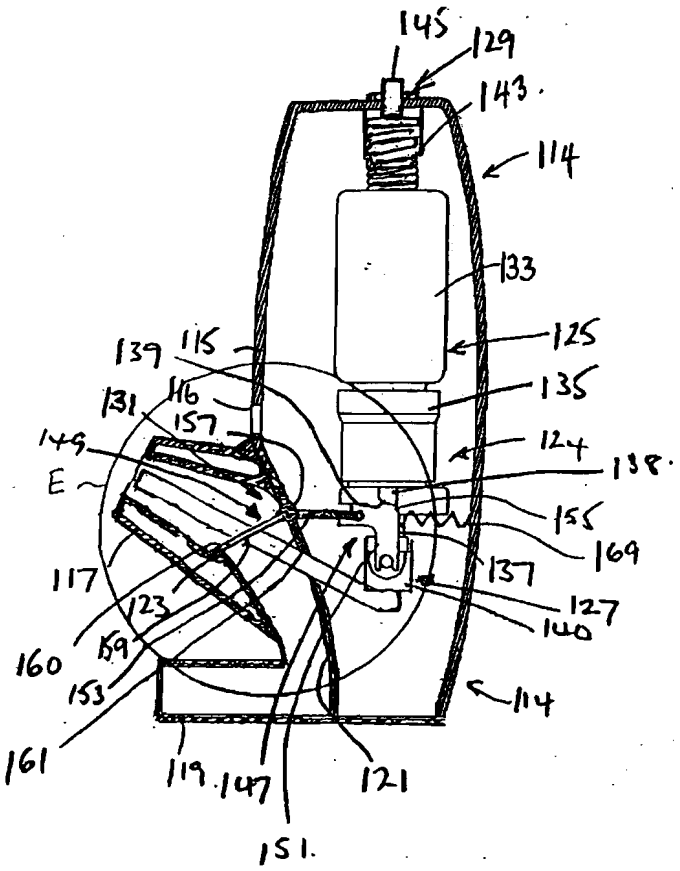

Fig. 12(a)

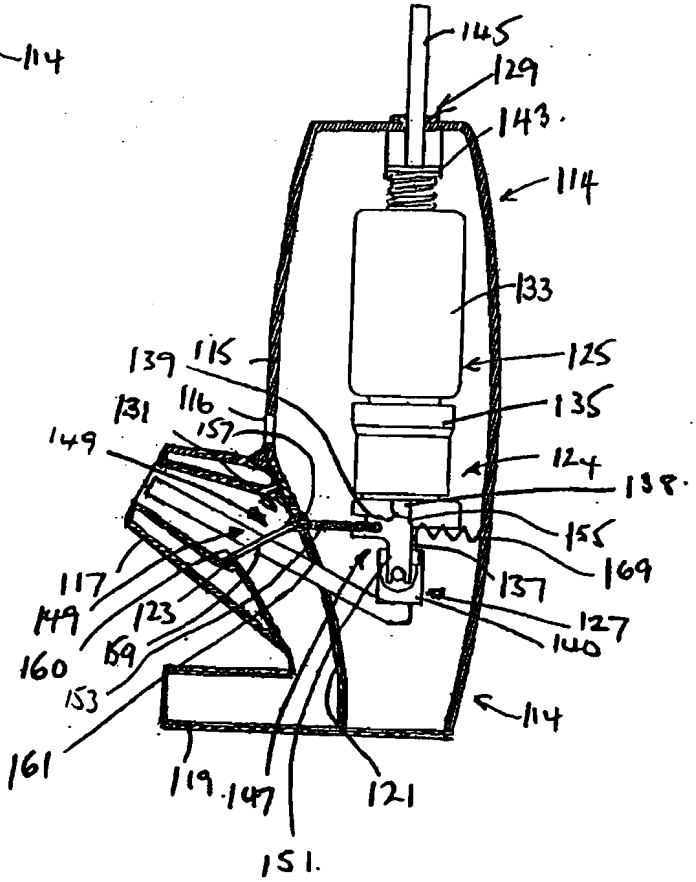

Fig. 12(b)

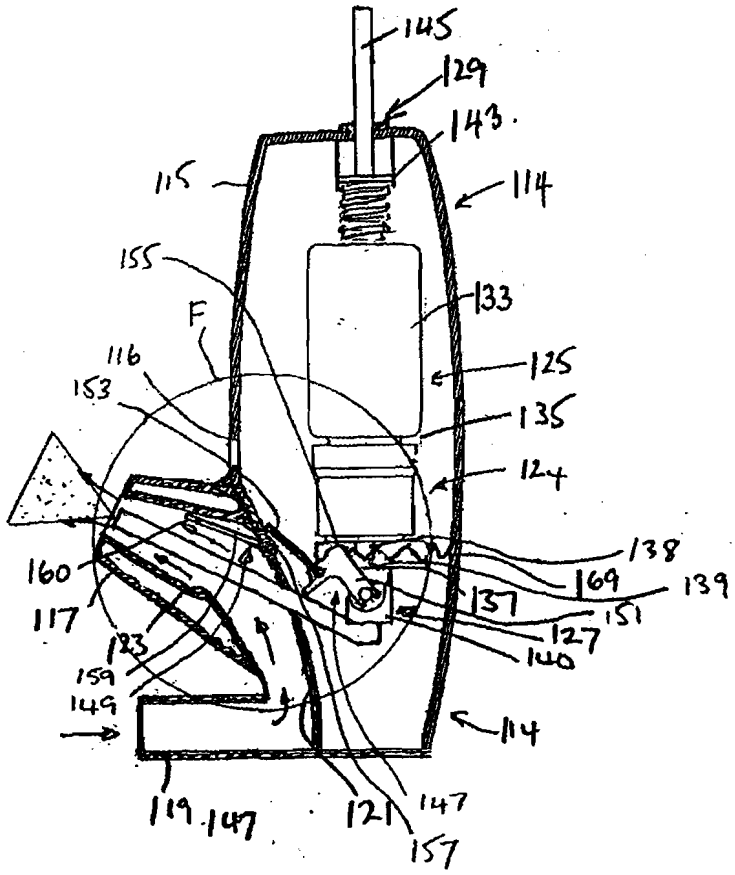
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Fig. 12(c)

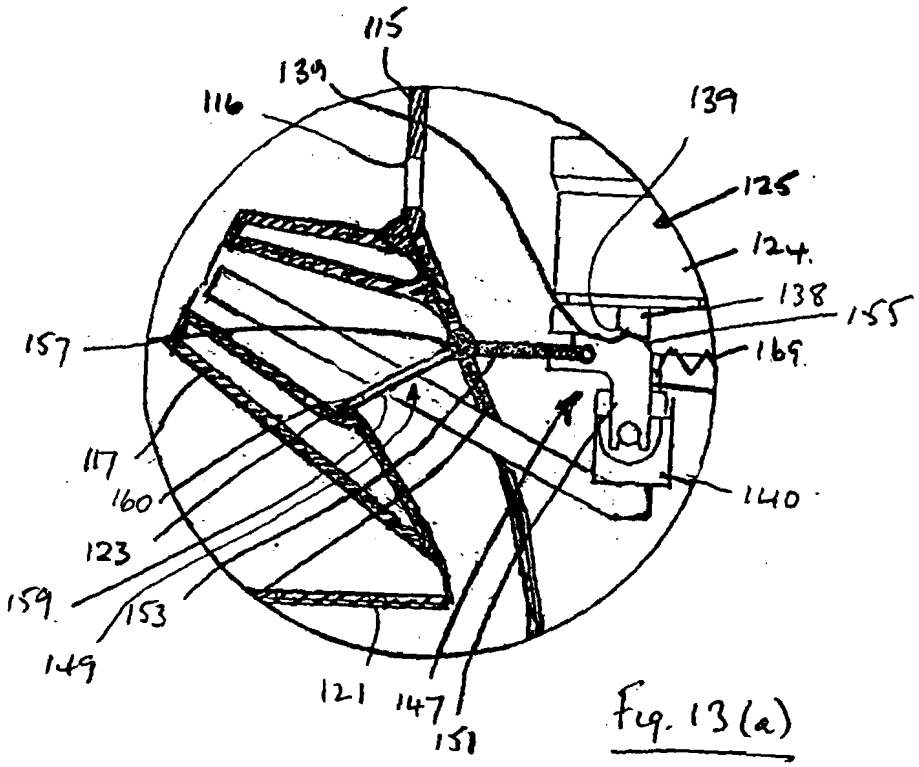


Fig. 13(a)

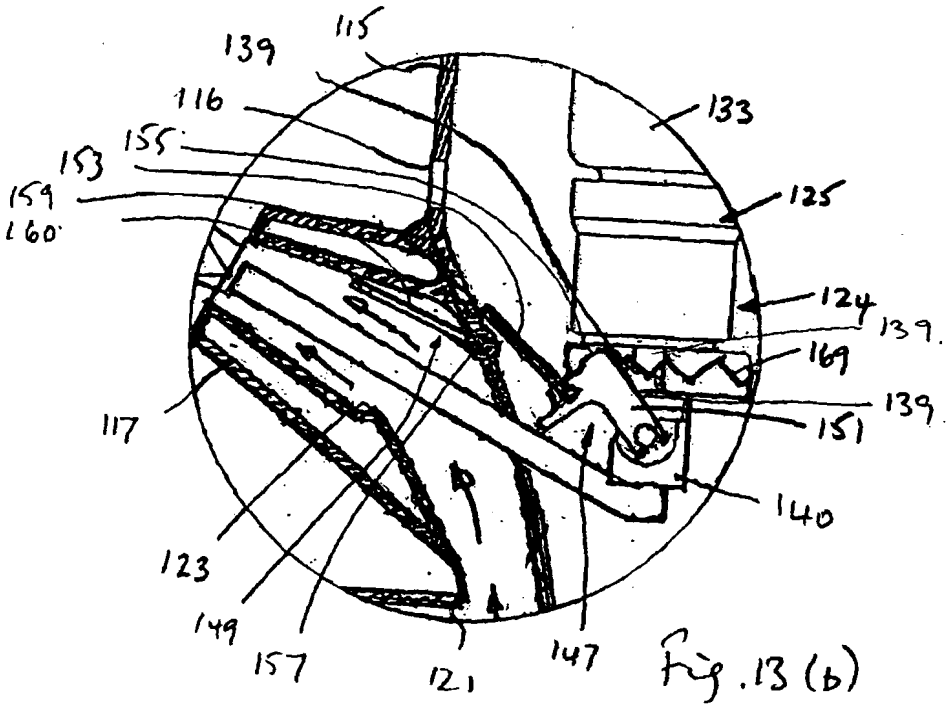
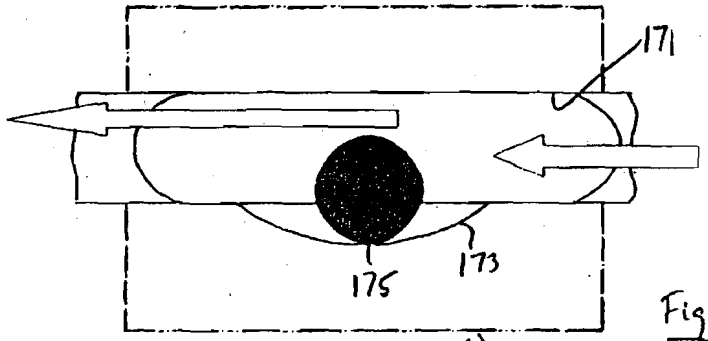


Fig. 13(b)



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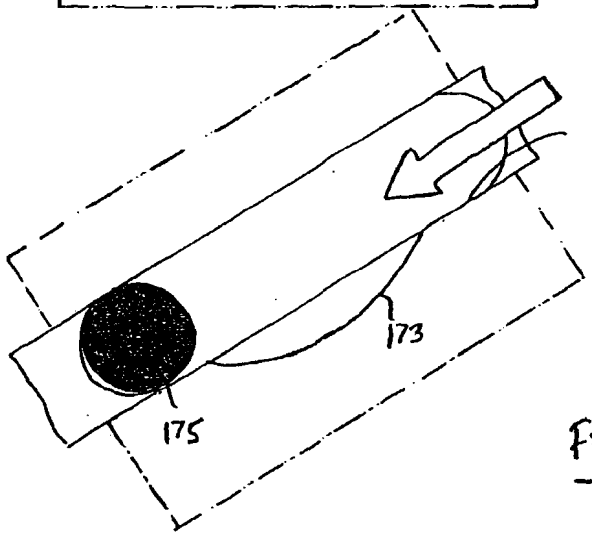

Fig. 14(b)

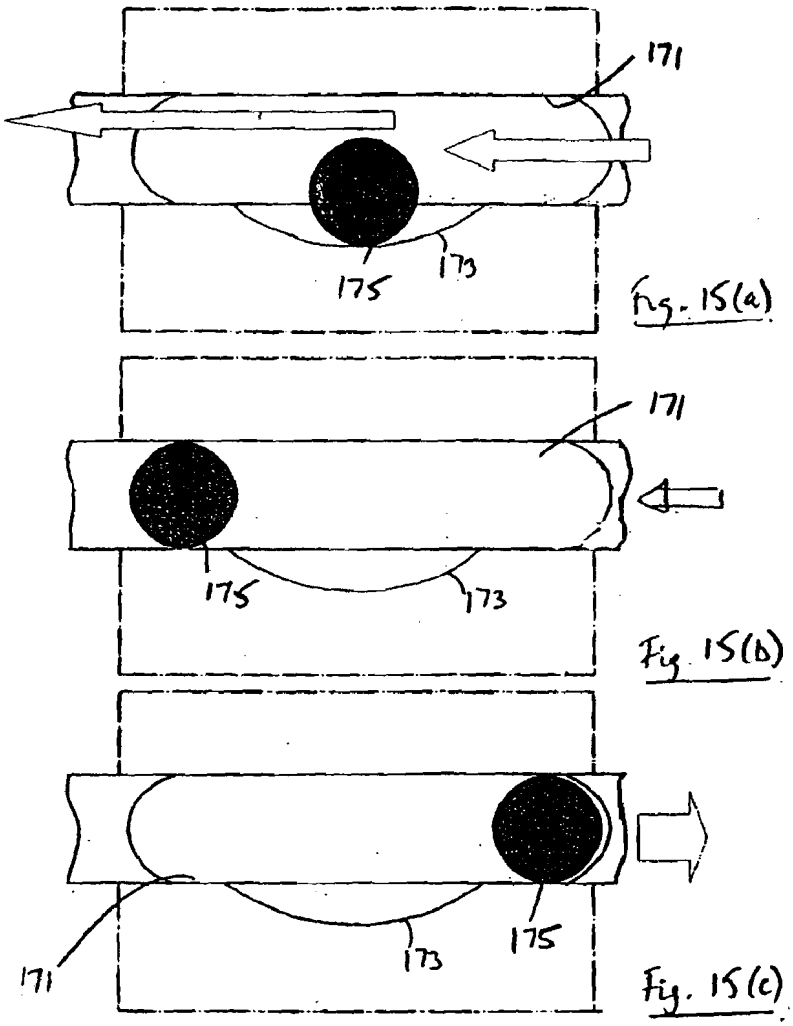

Fig. 15(a)

Fig. 15(b)

Fig. 15(c)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/03849

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 51672 A (DJUPESLAND PER GISLE) 8 September 2000 (2000-09-08) cited in the application the whole document and in particular page 29, line 22 - page 31, line 7; figure 9	1-12, 16-28, 32,36-42
A	US 5 355 873 A (TREYER WALTER ET AL) 18 October 1994 (1994-10-18) abstract	40-42
A	US 5 046 493 A (KROPKOWSKI JAMES ET AL) 10 September 1991 (1991-09-10) column 2, line 51 - line 54	1,32

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 January 2003	30/01/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lakkis, A

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/03849

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 43,44
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 43,44

See PCT Rule 6.2a

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 02/03849

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0051672 A	08-09-2000	AU 2822700 A	21-09-2000
		BR 0008650 A	26-12-2001
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US 5046493 A	10-09-1991	NONE	

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(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 April 2002 (18.04.2002)

PCT

(10) International Publication Number
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(51) International Patent Classification[7]: A61M 15/00, B05B 11/06

(21) International Application Number: PCT/GB01/04083

(22) International Filing Date:
12 September 2001 (12.09.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0025027.4 12 October 2000 (12.10.2000) GB

(71) Applicant *(for all designated States except US)*: **BESPAK PLC** [GB/GB]; Bergen Way, North Lynn Industrial Estate, King's Lynn, Norfolk PE30 2JJ (GB).

(72) Inventors; and

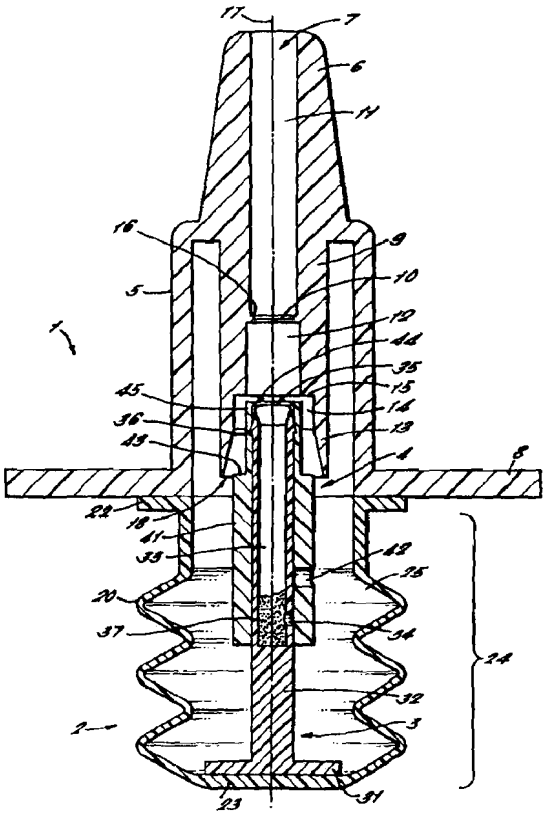
(75) Inventors/Applicants *(for US only)*: **WRIGHT, Andrew, David** [GB/GB]; 5 Malthouse Close, Heacham, King's Lynn, Norfolk PE31 7EH (GB). **POLLET, Hilde, Rachel, Maria** [GB/GB]; 3 St. James Street, King's Lynn, Norfolk PE30 5DA (GB). **HARRISON, Richard, Iain** [GB/GB]; Flat 6, Ufton Close, New Road, Bourne End, Buckinghamshire SL8 5BZ (GB).

(74) Agents: **BAYLISS, Geoffrey, Cyril** et al.; Boult Wade Tennant, Verulam Gardens, 70 Gray's Inn Road, London WC1X 8BT (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,

[Continued on next page]

(54) Title: DISPENSING APPARATUS



(57) Abstract: The present invention relates to a disposable dispensing apparatus for delivering a powdered product nasally or orally. The apparatus comprises a housing (1) defining an outlet (7) and a shaft (32) having a storage chamber (33) therein for a product provided with a first inlet (34) and a first outlet (35). A sheathing means (4) is slidably mounted on the shaft and has a second inlet (42) and a second outlet closed by a frangible membrane (44). There is also provided a variable volume means (2) operatively connected to the shaft. The shaft is movable, on operation of the variable volume means to reduce the variable volume so as to pressurise gas in an interior of the variable volume means, from an initial storage position in which the first and second inlets are out of alignment so as to close a gas flow path, to a dispensing position in which the first and second inlets are brought into alignment by action of the housing against the sheathing means. At the same time, the frangible membrane is ruptured by the shaft so as to open the gas flow path, such that pressurized gas from the interior of the variable volume means is discharged along the gas flow path comprising the first and second inlets, storage chamber, second outlet and first outlet, to thereby entrain powdered product and dispense it through the housing outlet.

WO 02/30500 A1

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) **Designated States** *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

DISPENSING APPARATUS

The present invention relates to a disposable dispensing apparatus for delivering a powdered product nasally or orally. In particular there is provided a single-use dry powder medicament inhaler for nasal use.

Single-use dry powder inhalers are known in the art. One such example is shown in US 5,683,361. However, the efficiency of delivery of the powdered product in this device is adversely affected due to the upper frangible membrane partially blocking the flow path after it has been ruptured. In other respects there is a need to reduce the manufacturing and assembly costs of single-dose dispensing apparatus.

The present invention provides a dispensing apparatus for dispensing a powdered product comprising: a housing defining an outlet, a shaft having a storage chamber therein for a powdered product provided with a first inlet and a first outlet, sheathing means slidably mounted on the shaft and having a second inlet and a second outlet closed by a frangible membrane, and variable volume means operatively connected to the shaft; wherein the shaft is moveable, on operation of the variable volume means to reduce the variable volume so as to pressurise gas in an interior of the variable volume means, from an initial storage position in which the first and second inlets are out of alignment so as to close a gas flow path, to a dispensing position, in which the first and second inlets are brought into alignment by action of the housing against the sheathing means and in which the frangible membrane is ruptured by the shaft so as to open the gas flow path, such that pressurised gas from the interior of the variable volume means is discharged along the gas flow path comprising the

first and second inlets, storage chamber, second outlet and first outlet, to thereby entrain powdered product and dispense it through the housing outlet.

Embodiments of the present invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

Figure 1 is a cross-sectional view of a first embodiment of dispensing apparatus according to the present invention in a 'storage' condition;

Figure 2 is a cross-sectional view of the apparatus of Figure 1 in a 'dispensing' condition;

Figure 3 is a cross-sectional view of a second embodiment of dispensing apparatus according to the present invention in a 'dispensing' condition; and

Figure 4 is a third embodiment of dispensing apparatus according to the present invention in a 'storage' condition.

Figures 5a and 5b show plan views of two variants of frangible membranes for use in the dispensing apparatus of the present invention; and

Figure 6 is a cross-sectional view of a part of the dispensing apparatus of the present invention showing a variant storage chamber inlet aperture.

As shown in Figures 1 and 2, a first embodiment of the present invention comprises a housing 1 having a generally cylindrical section 5, tip 6 and finger rests 8. The cylindrical section 5 of the housing 1 is provided with an internal, axially orientated, tubular extension 9. A bore of the tubular extension 9 is closed off part-way along its length by a first frangible membrane 10. The bore defines a duct 12 extending from the first frangible membrane 10 in a direction of an open end 18 of the tubular extension 9 and an outlet duct 11 extending from the first frangible membrane 10 in a direction of the tip 6.

The extremity of the outlet duct 11 distal the first frangible membrane 10 defines an outlet 7 in tip 6. Preferably the duct 12 and outlet duct 11 both extend along a longitudinal axis 17 of the housing 1.

The open end 18 of duct 12 is provided with a frusto-conically shaped mouth 13 leading to a bore portion 14 of enlarged diameter. The junction between the duct 12 and bore portion of enlarged diameter 14 defines an annular internal shoulder 15.

The finger rests 8 may be formed by a single annular flange extending from the cylindrical section 5 or by two or more separate flanges circumferentially spaced around the cylindrical section 5.

A bellows unit 2 is joined to the housing 1. The bellows unit 2 comprises an annular mounting flange 22 and an axially extending bellows portion 24 having a plurality of concertina formations 20 formed therein. An end of the bellows unit 2 distal the mounting flange 22 is closed off by an end face 23 defining a finger or thumb rest.

A probe 3 is provided within the bellows unit 2 and housing 1. The probe 3 comprises a cylindrical extension 32 which is mounted by means of a basal flange 31 to the inside of end face 23 so as to lie extending substantially along longitudinal axis 17. The cylindrical extension 32 comprises a hollow portion at an end distal the basal flange 31 defining a powder storage chamber 33. The distal end of the cylindrical extension 32 is shaped to form a piercing tip 35 and is provided with retaining barbs 36. A radially directed aperture 34 is provided in the wall of the cylindrical extension 32 communicating with the storage chamber 33.

A sheath 4 is slidably mounted on the cylindrical extension 32. The sheath 4 comprises a cylindrical portion 41 having a radially orientated aperture 42 therein and a reduced diameter portion 45 being closed

at one end by a second frangible membrane 44. The junction between the cylindrical portion 41 and reduced diameter portion 45 defines an external annular shoulder 43. The internal diameter of the sheath 4 is such that sliding movement between the sheath 4 and probe 3 is facilitated while maintaining a air-tight seal therebetween. Optionally sliding seal members, such as O-rings, may be provided between the sheath 4 and probe 3 to improve the seal integrity.

The powdered product to be dispensed is held in the storage chamber 33.

In a storage position, as shown in Figure 1, the sheath 4 is mounted on probe 3 with the piercing tip 35 in close proximity to or abutting against the second frangible membrane 44. In this position the radial apertures 34 and 42 are out of alignment and there is consequently no open path between an interior 25 of the bellows portion 24 and the storage chamber 33. Thus, the apertures 34 and 42, which together form an inlet valve, are in a 'closed' position.

The housing 1, probe 3 and sheath 4 are manufactured from polyethylene or polypropylene or similar material. Similarly, the frangible membranes 10, 44 are manufactured from polyethylene or polypropylene or similar material. Alternatively, the probe 3 may be manufactured from a metal such as stainless steel.

The bellows unit 2 is manufactured from polyethylene, polypropylene, a thermoplastic elastomer or other similarly flexible polymer. The unit 2 may be formed from as a single moulding of a single material. Alternatively, the unit 2 may be formed as a two-part moulding, each part being of a different material.

Advantageously, the materials of the dispensing apparatus lend themselves to easy and ready recycling.

In the preferred arrangement, the absence of any metallic or ceramic components reduces the cost of processing the recycled material.

Typically, the thickness of the frangible membranes 10, 44 is between 0.05 and 0.30 mm. As shown in Figures 5a and 5b, the first frangible membrane 10 may optionally be provided with one or more pre-formed lines of weakness to aid the rupturing of the membrane by the piercing tip 35. Figure 5a depicts a 'star' pattern of weaknesses and Figure 5b depicts a 'half-moon' pattern of weaknesses. In the same way the second frangible membrane 44 may be provided with lines of weakness.

Advantageously, the components of the dispensing apparatus are moulded. This leads to low levels of material waste. The current design allows for a low number of individual parts which reduces assembly time and cost. For example, the whole apparatus may be formed from only three components, the first component being the housing 1 including the first frangible membrane 10, the second component being the bellows unit 22 and probe 3 formed as a unitary part, and the third component being the sheath 4 including the second frangible membrane 44.

In use, a user holds the apparatus typically by means of two or more fingers positioned on the finger rests 8 and a thumb positioned on end face 23. The tip 6 is then inserted into the nose (or mouth if the apparatus is for pulmonary use). Inhalation at this stage is ineffective since the first frangible membrane 10 seals off the outlet duct 11.

The user depresses the end face 23 of the bellows unit 2 so as to move the probe 3 and sheath 4 axially into housing 1 in the direction of tip 6. Initially, the probe 3 and sheath 4 are free to move unhindered with the reduced diameter portion 45 of the sheath 4 being slidingly received in the duct 12. Further

movement of the probe 3 and sheath 4 brings the external shoulder 43 of the sheath 4 into contact with the internal shoulder 15 of the tubular extension 9. At this point, further inward movement of the sheath 4 relative to the tubular extension 9 is prevented. Continued inward movement of the probe 3 causes the piercing tip 35 of the probe 3 to pierce and break the second frangible membrane 44. Subsequent inward movement of the probe 3 then causes the piercing tip 35 to pierce and break the first frangible membrane 10 opening communication between the duct 12 and outlet duct 11. Advantageously, both of the frangible membranes 44, 10 are ruptured from below with the piercing means 35 moving relative to the membranes in the direction of tip 6. As a result the 'flap' of the membrane which is left after rupture is positioned above the membrane periphery such that as gas passes the membrane the 'flap' tends to be moved away from the hole formed in the membrane so as not to block the flow path unlike where a membrane is ruptured from above.

As the piercing tip 35 passes through the first frangible membrane 10 the barbs 36 or other snap-fit formations are engaged and retained with an annular lip 16 of the first frangible membrane 10, preventing retraction of the probe 3 in the direction of the bellows unit 2. Advantageously, the barbs 36 prevent any attempt at re-use of the dispensing apparatus and also provide a clear visual indication that the apparatus has been used.

The axial length of the reduced diameter portion 45 of the sheath 4 and the duct 12 can be chosen such that the first and second frangible membranes lie in close proximity at the point of rupture ensuring that the user feel a single, positive sensory signal that the storage chamber 33 has been opened.

Simultaneously with the first and second

membranes being ruptured, the relative axial movement of the sheath 4 and probe 3 causes the apertures 34 and 42 to come into alignment, opening the inlet valve of the storage chamber 33. The apparatus is now in the 'dispensing' position, as shown in Figure 2. In the dispensing position the inlet valve is open and the first and second frangible membranes are ruptured. Thus a continuous flow path is established between the interior 25 of the bellows portion 24 and the outlet 7. As a result air, pressurised during inward movement of the bellows unit's concertinas 20, is displaced from the interior 25 of the bellows portion 24, through the inlet valve formed by the apertures 34 and 42 and into the storage chamber 33 where it entrains the powdered product. The air and entrained product is then displaced through piercing tip 35, duct 12 and outlet duct 11 where it finally exits outlet 7. In this way the apparatus actively dispenses the powdered product so that the necessary inhalatory effort required by the user is reduced or even effectively eliminated.

The degree of compression and pressurisation of the air within the bellows unit 2 provides adequate energy to efficiently entrain and dispense the powdered product with little or no inhalatory effort by the user. Advantageously, this means that the apparatus may be used for dispensing products to users who can provide little inhalatory effort such as children or the elderly as well as to users who are unable to provide any inhalatory effort such as those who are unconscious.

Figure 3 shows a second embodiment of dispensing apparatus according to the present invention. Similar features to those described above with reference to the first embodiment have been designated with like reference numerals and will not be described in further detail except where they differ in form or

function.

The housing 1 of the second embodiment is modified such that the tip 6 and cylindrical section 5 are formed as a single body of substantially constant cross-section. A slight tapering of the tip 6 is preferably provided for the comfort of the user.

The tubular extension 9 is dispensed with. Instead an internal wall 19 of the tip 6 and cylindrical section 5 defines duct 12, outlet duct 11 and internal shoulder 15.

The storage chamber 33 is provided with a hemispherically shaped lower end 38 which is believed to lead to more efficient entrainment and removal of the powdered product from the storage chamber 33. Alternatively the lower end 38 may be V-shaped or U-shaped in cross-section.

The mounting flange 22 is received in an annular socket defined on the finger rests 8 by annular rim 26 leading to a more secure attachment.

Likewise, the basal flange 31 of the probe 3 is received in a socket defined by annular rim 27 formed on the inner surface of end face 23.

The operation of the second embodiment is substantially the same as that of the first embodiment.

The second embodiment has a less complicated form leading to easier moulding of the component parts.

Figure 4 shows a third embodiment of dispensing apparatus according to the present invention. Similar features to those described above with reference to the second embodiment have been designated with like reference numerals and will not be described in further detail except where they differ in form or function.

In the third embodiment the first frangible membrane 10 is replaced by a second bellows unit 50. The second bellows unit 50 comprises a bellows section

having a number of concertina formations 51, and two sleeve portions 52 and 53. The first sleeve portion 52 is push-fit into mouth 13 of housing 1. The second sleeve portion 53 is slid as a push-fit over the outer surface of the sheath 4. A snap-fit may be provided between the second sleeve portion 53 and the sheath 4 to aid retention of the sleeve portion on the sheath.

The tip 6 may be profiled so as to more comfortably fit into the nose of the user.

In other ways the third embodiment is similar to the second embodiment.

In use, displacement of the end face 23 by the user cause the probe 3 to be moved inwardly in the direction of tip 6 as with the previous embodiments. Fluid communication between the interior 25 of the bellows portion 24 and the outlet 7 is prevented by the fluid tight seals between the sleeve portions 52, 53 of the second bellows unit 50 and respectively the mouth 13 and sheath 4. The flexibility of the concertina formations 51 of the second bellows unit 50 accommodates the inward movement of the probe 3. Subsequent operation of the apparatus is the same as for the previous embodiments with the piercing tip rupturing the frangible membrane 44.

Figure 6 shows a variant of the aperture 34 wherein the aperture is directed so as to have a component in the axial direction as well as the radial direction. In this way the air entering the storage chamber 33 is directed towards the closed lower end 38 of the chamber 33 so as to more efficiently entrain the powdered product 37. Alternatively, the inlet aperture 34 may be angled so as to have components in the radial, axial and circumferential directions such that air entering the storage chamber 33 is directed towards the lower end 38 with a 'spiralling' motion. In any of these arrangements the inlet aperture 34 may be positioned so as to be covered or uncovered by the

powdered product in the storage condition. More than one aperture 34 may be provided.

Alternatively, the inlet aperture 34 may be positioned in the lower end 38 of the storage chamber 33 such that air entering the chamber enters underneath the powdered product and is directed axially along the chamber 33 towards the piercing tip 35. In a yet further alternative, the powdered product may be suspended on a mesh within the storage chamber 33 such that air entering the storage chamber 33 enters below the mesh and entrains the powdered product as it passes through the mesh.

Optionally, the storage chamber 33 may be provided with rifling grooves or similar along its length to impart a 'spiralling' motion to the air and entrained product as it passes along the chamber towards the piercing tip 35.

The bellows unit 2 may be substituted by a tube with weakened sections, a bulbous sack or a memory returning form.

The finger rests 8 may incorporate a plurality of axially directed flanges aligned co-axially around the bellows unit 2 to form a guard preventing accidental depression of the bellows unit 2.

The dispensing apparatus may be provided in a sterile package such as a foil packet for reasons of hygiene. Alternatively, a cap may be provided to cover and close of outlet 7 before use.

While the apparatus has been specifically described for use as a nasal apparatus, it may equally be used for oral delivery of powdered products. In such a case tip 6 may be advantageously replaced by a mouthpiece.

Features of the invention which have been described in the context of separate embodiments may also be provided in combination in a single embodiment. Conversely, the features of the invention

which have been described in a single embodiment may be provided separately or in any suitable sub-combination.

Claims:

1. Dispensing apparatus for dispensing a powdered product comprising:

a housing defining an outlet,

a shaft having a storage chamber therein for a powdered product provided with a first inlet and a first outlet,

sheathing means slidably mounted on the shaft and having a second inlet and a second outlet closed by a frangible membrane, and

variable volume means operatively connected to the shaft;

wherein the shaft is moveable, on operation of the variable volume means to reduce the variable volume so as to pressurise gas in an interior of the variable volume means, from an initial storage position in which the first and second inlets are out of alignment so as to close a gas flow path, to a dispensing position, in which the first and second inlets are brought into alignment by action of the housing against the sheathing means and in which the frangible membrane is ruptured by the shaft so as to open the gas flow path, such that pressurised gas from the interior of the variable volume means is discharged along the gas flow path comprising the first and second inlets, storage chamber, second outlet and first outlet, to thereby entrain powdered product and dispense it through the housing outlet.

2. Dispensing apparatus as claimed in claim 1 wherein the housing further comprises means for sealing the housing outlet in the storage position.

3. Dispensing apparatus as claimed in claim 2 wherein the sealing means is a second frangible membrane which is ruptured by the shaft as the shaft

moves from the storage position to the dispensing position.

4. Dispensing apparatus as claimed in claim 2 wherein the sealing means is a flexible member sealing between the sheathing means and the housing.

5. Dispensing apparatus as claimed in any preceding claim wherein the shaft is adapted such that the or each frangible membrane is ruptured by the shaft moving relative to the frangible membrane in the direction of the housing outlet.

6. Dispensing apparatus as claimed in any preceding claim wherein the or each frangible membrane comprises one or more pre-formed lines of weakness.

7. Dispensing apparatus as claimed in any preceding claim wherein the or each frangible membrane is 0.05 to 0.30 mm thick.

8. Dispensing apparatus as claimed in any preceding claim wherein as the shaft moves from the storage position to the dispensing position the sheathing means abuts an inwardly directed shoulder of the housing.

9. Dispensing apparatus as claimed in claim 8 wherein the inwardly directed shoulder is formed within a tubular extension of the housing.

10. Dispensing apparatus as claimed in claim 9 wherein a mouth of the tubular extension which receives the shaft as it moves from the storage position to the dispensing position has a frusto-conical form.

11. Dispensing apparatus as claimed in any of claims 8 to 10 wherein the sheathing means comprises an outwardly directed shoulder which abuts the inwardly directed shoulder of the housing as the shaft moves from the storage position to the dispensing position.

12. Dispensing apparatus as claimed in any preceding claim wherein the sheathing means forms a sliding seal against the shaft.

13. Dispensing apparatus as claimed in claim 12 wherein one or more sealing members are provided between the sheathing means and the shaft.

14. Dispensing apparatus as claimed in any preceding claim wherein the axis of the first inlet of the shaft is radially directed.

15. Dispensing apparatus as claimed in any of claims 1 to 14 wherein the axis of the first inlet of the shaft is axially directed.

16. Dispensing apparatus as claimed in any of claims 1 to 14 wherein the axis of the first inlet of the shaft is directed to have both radial and axial components.

17. Dispensing apparatus as claimed in any of claims 1 to 14 wherein the axis of the first inlet of the shaft is directed to have radial, axial and circumferential components.

18. Dispensing apparatus as claimed in any preceding claim wherein the storage chamber has more than one inlet.

19. Dispensing apparatus as claimed in claim 18

wherein the inlets are displaced axially relative to one another along the length of the storage chamber.

20. Dispensing apparatus as claimed in any preceding claim wherein the first inlet of the shaft is located above the level of powdered product stored within the storage chamber.

21. Dispensing apparatus as claimed in any of claims 1 to 19 wherein the first inlet of the shaft is located below the level of powdered product stored within the storage chamber.

22. Dispensing apparatus as claimed in any preceding claim wherein the storage chamber in the shaft comprises a hemi-spherical, V-shaped or U-shaped base.

23. Dispensing apparatus as claimed in any preceding claim wherein the internal walls of the storage chamber are rifled.

24. Dispensing apparatus as claimed in any preceding claim wherein the shaft comprises piercing means for rupturing the or each frangible membrane.

25. Dispensing apparatus as claimed in any preceding claim wherein the shaft comprises means for engaging the housing and retaining the shaft relative to the housing when in the dispensing position.

26. Dispensing apparatus as claimed in claim 25 wherein the retaining means are one or more reverse-directed projections adjacent the outlet of the shaft.

27. Dispensing apparatus as claimed in any preceding claim wherein the variable volume means is a bellows.

28. Dispensing apparatus as claimed in any preceding claim wherein the variable volume means is a flexible sac.

29. Dispensing apparatus as claimed in any preceding claim wherein the variable volume means is a tube with weakened sections.

30. Dispensing apparatus as claimed in any preceding claim wherein at least the housing is a moulded component.

31. Dispensing apparatus as claimed in claim 30 wherein the shaft is a moulded component.

32. Dispensing apparatus as claimed in claim 30 or 31 wherein the sheathing means is a moulded component.

33. Dispensing apparatus as claimed in any preceding claim formed from on or more of polyethylene, polypropylene or other thermoplastic elastomer.

34. Dispensing apparatus as claimed in any preceding claim adapted for nasal delivery of powdered products.

35. Dispensing apparatus as claimed in any of claims 1 to 33 adapted for oral delivery of powdered products.

36. Dispensing apparatus substantially as hereinbefore described with reference to and as shown in the accompanying drawings.

FIG. 1.

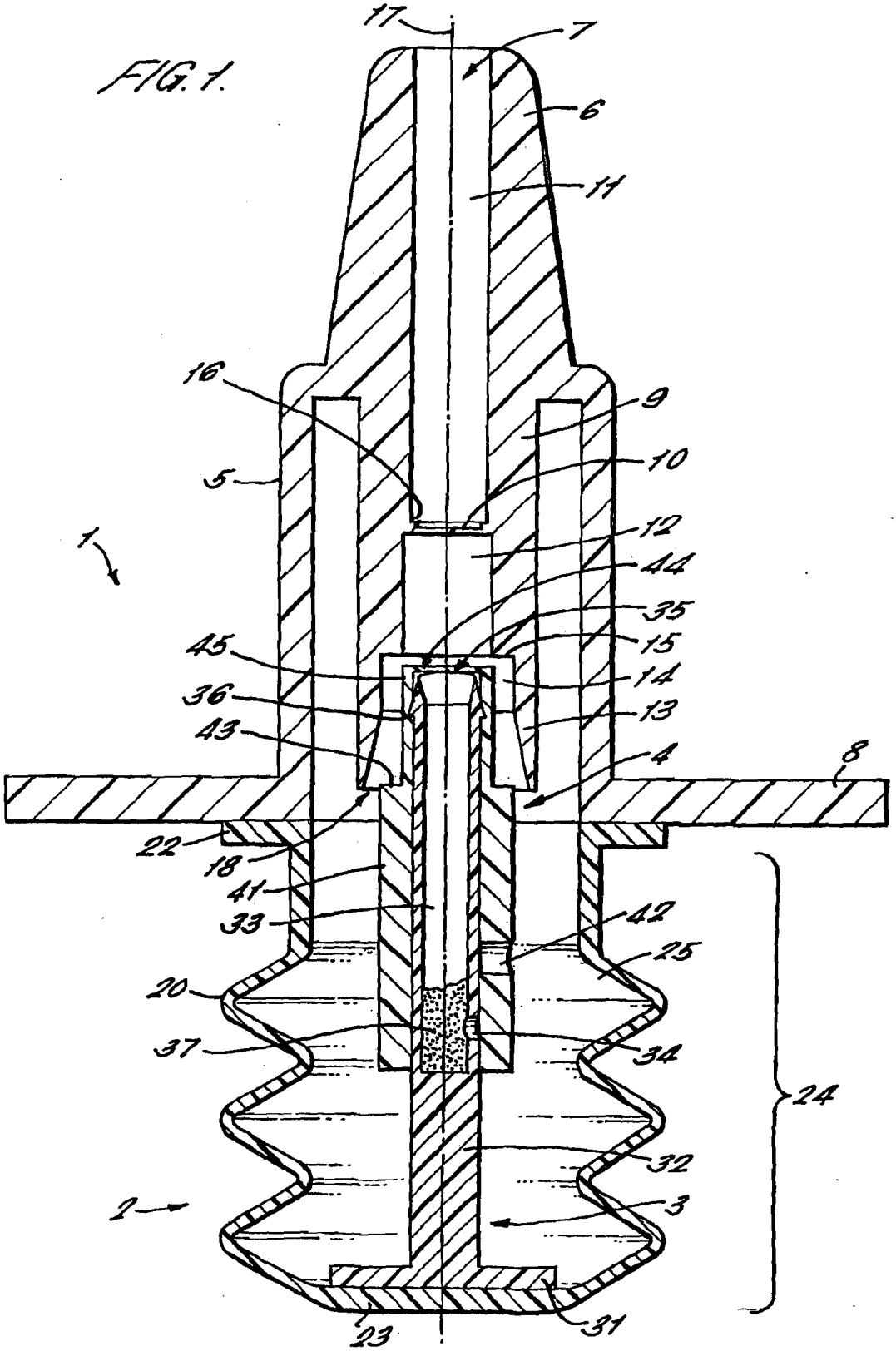

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FIG. 2.

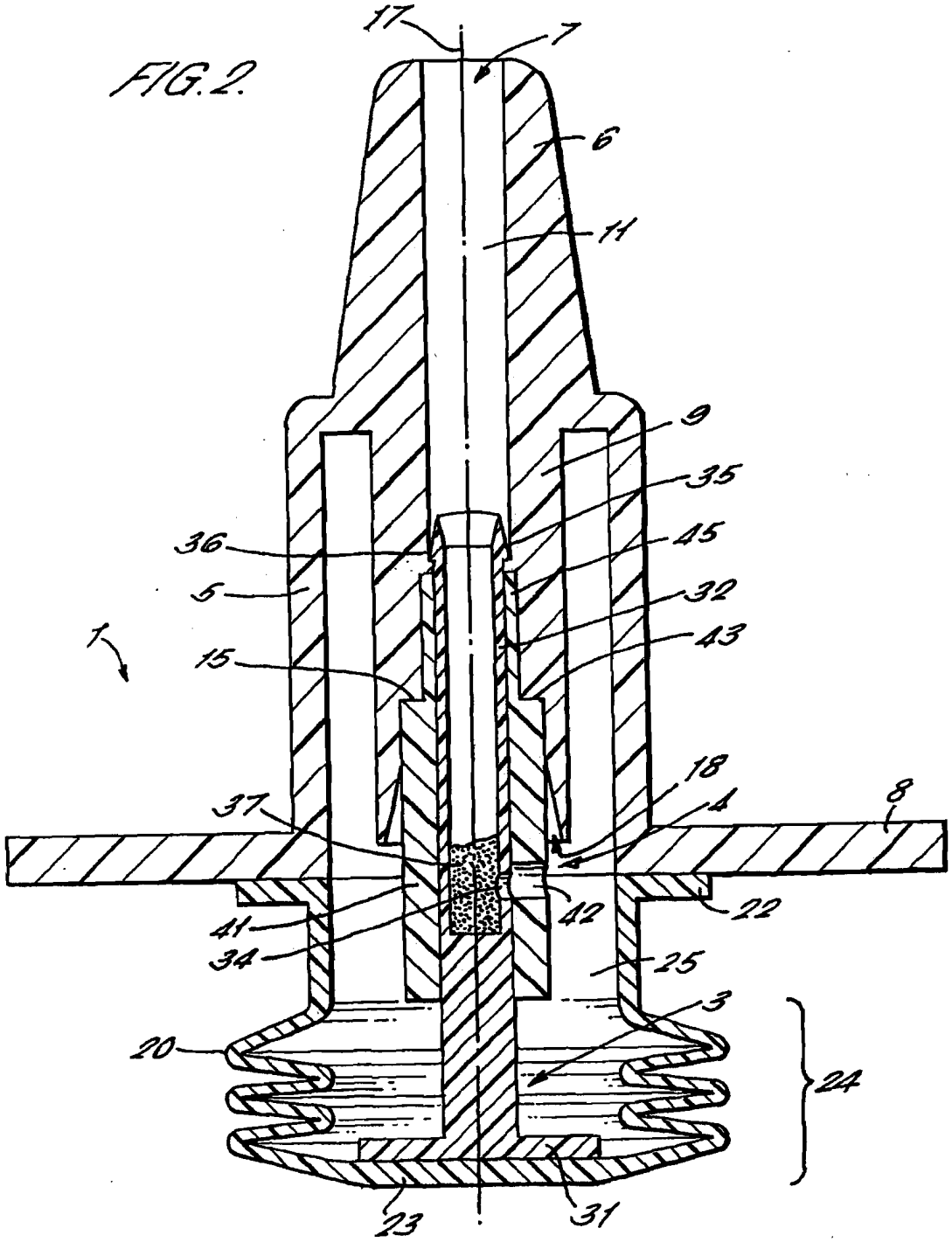

FIG.3.

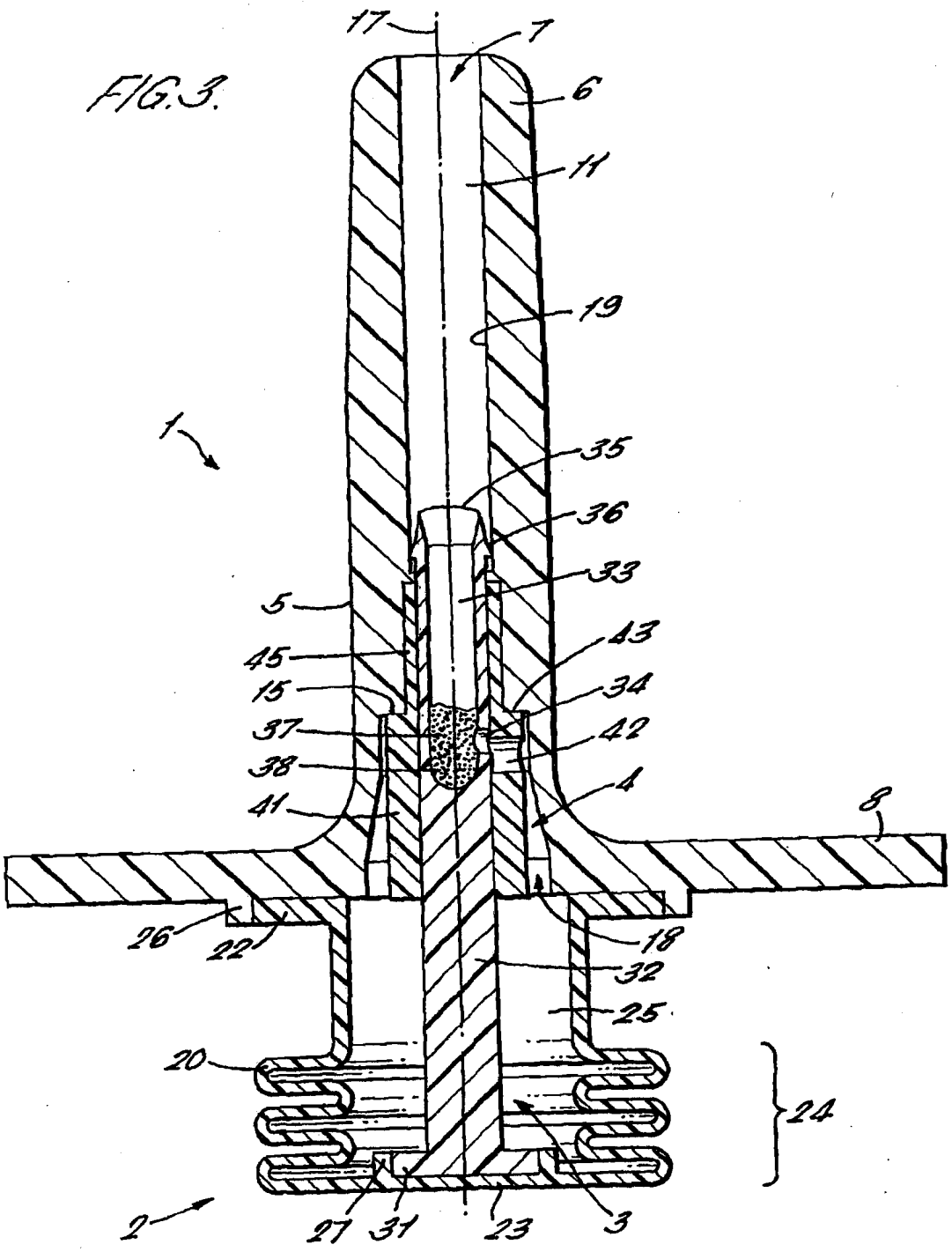
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FIG.4.

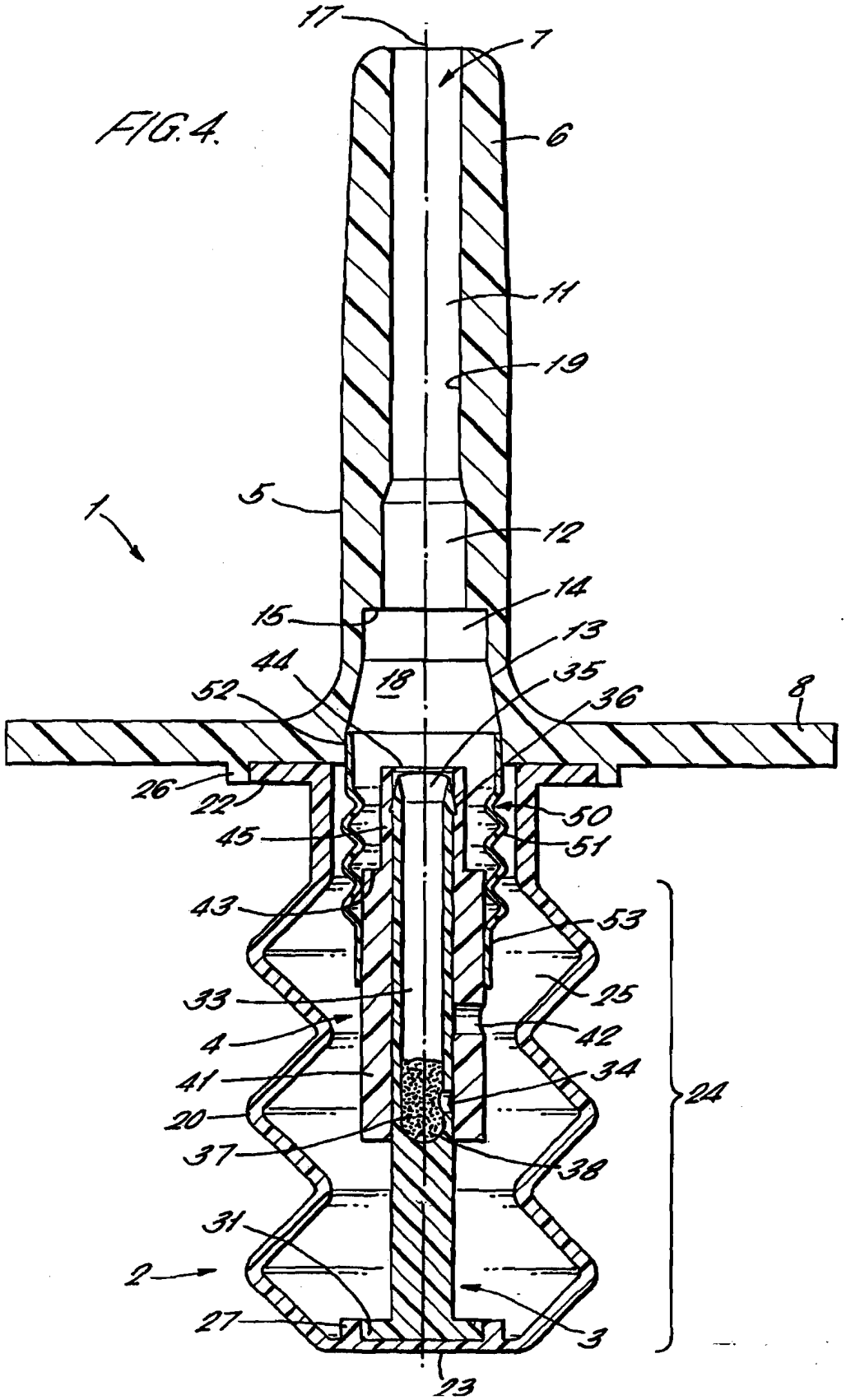
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FIG. 5a.

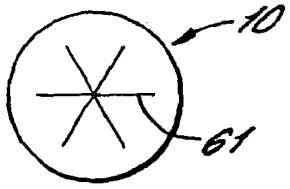


FIG. 5b.

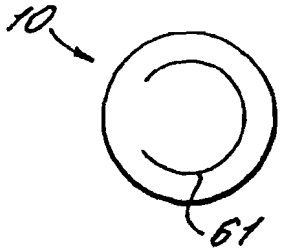
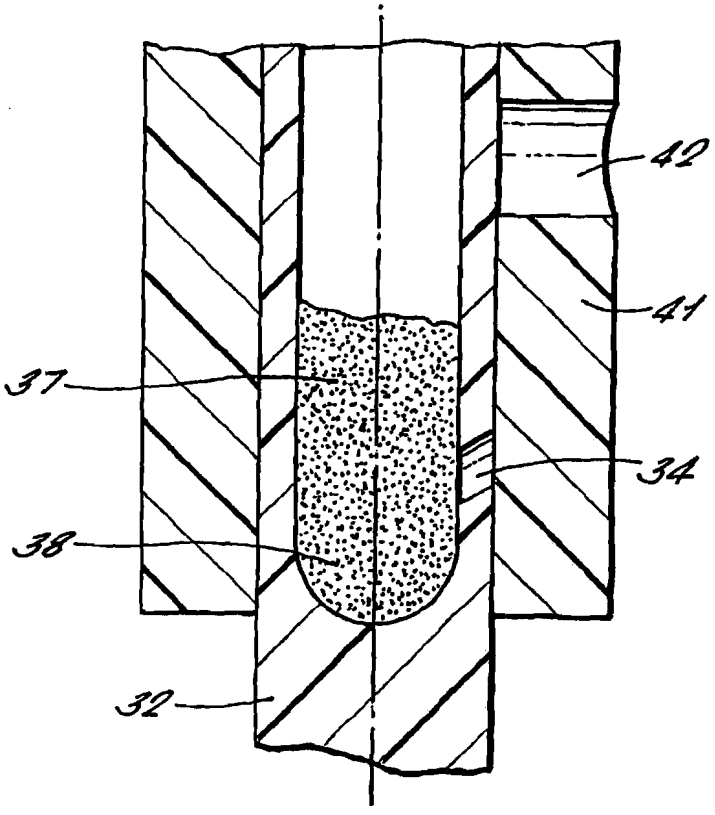


FIG. 6.



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/04083

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/00 B05B11/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M B05B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 683 361 A (ELK SVEND ET AL) 4 November 1997 (1997-11-04) cited in the application abstract; figure 1	1
A	WO 92 06727 A (NOVONORDISK AS) 30 April 1992 (1992-04-30) abstract; figure 1	1
A	WO 99 46055 A (GUIFFRAY JEAN LOUIS ;VALOIS SA (FR); BRUNA PASCAL (FR)) 16 September 1999 (1999-09-16)	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 November 2001	27/11/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lakkis, A

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 36

see Rule 6.2a PCT

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 01/04083

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		WO 9946055 A1	16-09-1999

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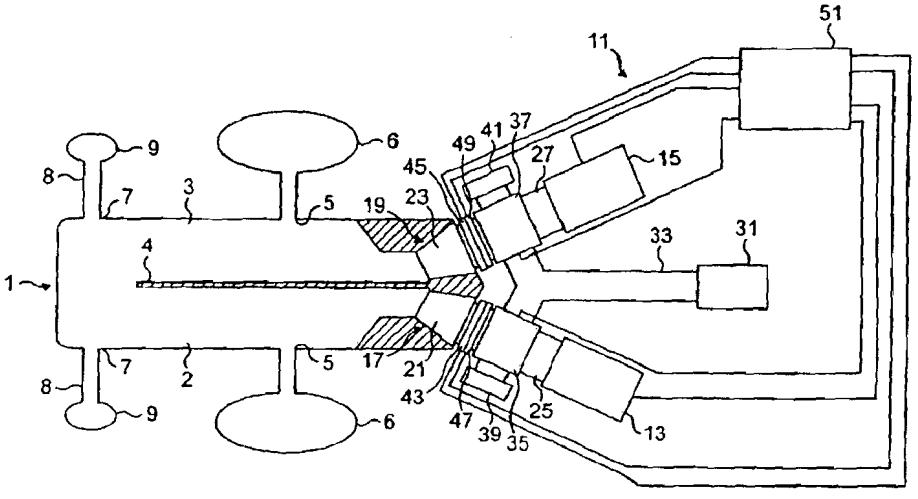

(57) Abstract: A nasal delivery device (11) for delivering substance to a nasal airway (1) of a subject, comprising: first and second nosepiece units (17, 19), each including a nosepiece (21, 23) for fitting to respective nostrils of a subject; at least one substance supply unit (13, 15) for supplying substance for delivery to the nasal airway (1) of the subject; and a valve unit (35, 37) for selectively fluidly connecting the at least one substance supply unit (13, 15) alternately to respective ones of the nosepiece units (17, 19).

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NASAL DEVICES

The present invention relates to a nasal delivery device for and a method of delivering substance, in particular one of a liquid, as a suspension or solution, or a powder containing a medicament, especially systemic or topical pharmaceuticals, or a vaccine to the nasal airway of a subject.

Referring to Figure 1, the nasal airway 1 comprises the two nasal cavities 2, 3 separated by the nasal septum 4, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 5 connected to the paranasal sinuses 6 and the tubal ostia 7 connected to the tuba auditiva 8 and the middle ears 9, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx, the oral cavity and the lower airway, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx and the oral cavity by opening and closing of the oropharyngeal velum.

There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants

have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitionin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa advantageously provides for rapid systemic uptake.

Nasal delivery is also expected to be advantageous for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and also other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

It is also expected that nasal delivery could provide an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

Furthermore, it is expected that nasal delivery using the nasal delivery technique of the present invention will prove effective in the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is

possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

Also, it is expected that the nasal delivery technique of the present invention will allow for the effective delivery of vaccines.

Aside from the delivery of medicaments and vaccines, the irrigation of the nasal mucosa with liquids, in particular saline solutions, is commonly practised to remove particles and secretions, as well as to improve the mucociliary activity of the nasal mucosa. These solutions can be used in combination with active pharmaceuticals.

For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse effects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

WO-A-00/51672 discloses a delivery device for delivering substance, in particular a medicament, in a bi-directional flow through the nasal cavities, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril. This bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

It is an aim of the present invention to provide an improved nasal delivery device for and method of delivering substance to the nasal airway of a subject.

In one aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: first and second nosepiece units, each including a nosepiece for fitting to respective nostrils of a subject; at least one substance supply unit for supplying substance for delivery to the nasal airway of the subject; and a valve unit for selectively fluidly connecting the at least one substance supply unit alternately to respective ones of the nosepiece units.

Preferably, the delivery device further comprises: a mouthpiece through which the subject in use exhales.

Preferably, the delivery device further comprises: a gas supply channel for supplying a gas flow for entraining substance supplied by the at least one substance supply unit.

In one embodiment the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the delivery device further comprises: a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

Preferably, the gas supply unit is an exhalation breath actuatable unit which is fluidly connected to the mouthpiece such as to be actuated on exhalation by the subject.

In one embodiment the valve unit is configured alternately fluidly to connect one of the nosepiece units to the at least one substance supply unit and vent the other of the nosepiece units, such that, where the gas flow is at a driving pressure which is such as to cause the gas flow to flow around the posterior margin of the nasal septum and through the nasal airway, the gas flow delivered through the one nosepiece unit is vented through the other nosepiece unit.

Preferably, the delivery device further comprises: at least one flow resistor to which the other nosepiece unit is vented.

In one embodiment the at least one flow resistor has a fixed flow resistance for providing a fixed flow resistance to the gas flow.

In another embodiment the at least one flow resistor is a progressive resistor for progressively providing an increasing flow resistance to the gas flow.

Preferably, the progressive resistor comprises an expandable member which provides a progressively increasing resistance to the gas flow.

Preferably, the delivery device further comprises: a control unit for controlling the valve unit such as to provide for alternate delivery of substance through respective ones of the first and second nosepiece units.

In one embodiment the delivery device comprises: a single substance supply unit for supplying substance for delivery alternately to respective ones of the first and second nosepiece units.

In another embodiment the delivery device comprises: first and second substance supply units for supplying substance for delivery to respective ones of the first and second nosepiece units.

Preferably, the valve unit comprises first and second valves, each being fluidly connected to a respective one of the first and second nosepiece units.

In another aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: fitting first and second nosepiece units to respective nostrils of a subject; and delivering substance alternately through respective ones of the nosepiece units.

Preferably, the method further comprises the step of: exhaling through a mouthpiece during delivery of substance.

Preferably, substance is delivered in a gas flow.

In one embodiment the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the gas flow is a gas flow separate to an exhalation breath of the subject.

In one embodiment substance is delivered alternately through the nosepiece units and the other of the nosepiece units is vented, such that, where the gas flow is at a driving pressure which is such as to cause the gas flow to flow around the posterior margin of the nasal septum and through the nasal airway, the gas flow delivered through the one nosepiece unit is vented through the other nosepiece unit.

Preferably, the gas flow is vented through a flow resistor.

In one embodiment the flow resistor has a fixed flow resistance and provides a fixed flow resistance to the gas flow.

In another embodiment the flow resistor is a progressive resistor which provides a progressively increasing flow resistance to the gas flow.

Preferably, the progressive resistor comprises an expandable member which provides a progressively increasing resistance to the gas flow.

In one embodiment substance is supplied from a single substance supply unit.

In another embodiment substance is supplied to the first and second nosepiece units from respective ones of first and second substance supply units.

In a further aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: at least one delivery unit for delivering substance to a nasal airway of a subject; and a gas supply unit for applying a varying pressure in the nasal airway of the subject.

Preferably, the gas supply unit is configured to cycle the pressure in the nasal airway of the subject.

More preferably, the gas supply unit is configured to provide an alternating pressure in the nasal airway of the subject.

Preferably, the delivery device further comprises: a mouthpiece through which the subject in use exhales.

More preferably, the gas supply unit is an exhalation breath actuatable unit which is fluidly connected to the mouthpiece such as to be actuated on exhalation by the subject.

In yet another aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: delivering substance to a nasal airway of a subject; and applying a varying pressure in the nasal airway of the subject.

Preferably, the step of applying a varying pressure in the nasal airway of the subject comprises the step of: cycling the pressure in the nasal airway of the subject.

More preferably, the step of applying a varying pressure in the nasal airway of the subject comprises the step of: alternating the pressure in the nasal airway of the subject.

Preferably, the method further comprises the step of: exhaling through a mouthpiece during delivery of substance.

In a yet further aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: at least one delivery unit for delivering substance to a nasal airway of a subject; and a gas supply unit for alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

Preferably, the delivery device further comprises: a mouthpiece through which the subject in use exhales.

In still yet another aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: delivering substance to a nasal airway of a subject; and alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

Preferably, the method further comprises the step of: exhaling through a mouthpiece during delivery of substance.

In a still yet further aspect the present invention provides an interface member for attachment to a nasal delivery device, comprising, as an integral element, at least one nosepiece for fitting to a nostril of a subject and a mouthpiece through which the subject in use exhales.

Preferably, the interface member comprises first and second nosepieces for fitting to respective nostrils of a subject

Preferably, the interface member is a disposable element.

In one embodiment the mouthpiece comprises a tubular section through which the subject in use exhales.

In another embodiment the mouthpiece includes a flexible member which is deflectable on exhalation into the mouthpiece.

Preferably, the mouthpiece comprises a cavity into which the subject in use exhales, with a part of the cavity being defined by the flexible member.

Preferably, the flexible member comprises a resilient member.

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figure 1 schematically illustrates the nasal airway of a human subject;

Figure 2(a) schematically illustrates a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 2(b) illustrates the nasal delivery device of Figure 2(a) in a first, delivery configuration;

Figure 2(c) illustrates the nasal delivery device of Figure 2(a) in a second, delivery configuration;

Figure 3(a) schematically illustrates a nasal delivery device in accordance with a second embodiment of the present invention;

Figure 3(b) illustrates the nasal delivery device of Figure 3(a) in a first, delivery configuration;

Figure 3(c) illustrates the nasal delivery device of Figure 3(a) in a second, delivery configuration;

Figure 4(a) schematically illustrates a nasal delivery device in accordance with a third embodiment of the present invention;

Figure 4(b) illustrates the nasal delivery device of Figure 4(a) in a first, delivery configuration;

Figure 4(c) illustrates the nasal delivery device of Figure 4(a) in a second, delivery configuration;

Figure 5(a) schematically illustrates a nasal delivery device in accordance with a fourth embodiment of the present invention;

Figure 5(b) illustrates the nasal delivery device of Figure 5(a) in a first, delivery configuration; and

Figure 5(c) illustrates the nasal delivery device of Figure 5(a) in a second, delivery configuration.

Figures 2(a) to (c) illustrate a nasal delivery device 11 in accordance with a first embodiment of the present invention.

The delivery device 11 comprises first and second substance supply units 13, 15 for supplying metered doses of substance. In preferred embodiments the substance comprises a medicament, especially systemic or topical pharmaceuticals, or a vaccine.

In this embodiment the substance supply units 13, 15 comprise aerosol canisters for delivering metered volumes of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing substance, either as a suspension or solution.

Each of the substance supply units 13, 15 is primeable, in this embodiment by loading a biasing element, and includes a release mechanism, in this embodiment electrically-operated, which, when triggered, releases the biasing element and actuates the respective substance supply unit 13, 15 to deliver a metered dose of substance.

In an alternative embodiment the substance supply units 13, 15 could comprise mechanical delivery pumps, in particular liquid delivery pumps or powder delivery pumps, which deliver metered doses of substance on actuation thereof.

In another alternative embodiment the substance supply units 13, 15 could comprise dry powder delivery units which deliver metered doses of substance, as a dry powder, on actuation thereof.

In yet another alternative embodiment the substance supply units 13, 15 could comprise nebulizers which deliver metered doses of substance, as an aerosol spray, on actuation thereof.

The delivery device 11 further comprises first and second nosepiece units 17, 19 for fitting to respective ones of the nostrils of a subject which are fluidly connected to respective ones of the first and second substance supply units 13, 15. In this embodiment the nosepiece units 17, 19 each comprise a nosepiece 21, 23 for fitting to respective ones of the nostrils of a subject and a flow channel 25, 27 which fluidly connects the respective ones of the nosepieces 21, 23 and the substance supply units 13, 15. In this embodiment the nosepieces 21, 23 are replaceable elements.

The delivery device 11 further comprises a mouthpiece 31 which is gripped by the lips of a subject and through which the subject exhales. In this embodiment the mouthpiece 31 is a replaceable element. In a preferred embodiment the nosepieces 21, 23 and the mouthpiece 31 are integrally formed as a single element such as to allow for replacement after use. In this way, the delivery device 11 can be used to deliver substance to many different subjects and yet avoid cross-contamination from subject to subject.

The delivery device 11 further comprises a gas supply channel 33 which is fluidly connected to the mouthpiece 31.

The delivery device 11 further comprises a valve unit which comprises first and second valves 35, 37 which are disposed in respective ones of the flow channels 25, 27 of the first and second nosepiece units 17, 19 and fluidly connected to the gas supply channel 33 such as to provide for the selective communication of one of the nosepieces 21, 23 with the mouthpiece 31 and the respective one of the substance supply units 13, 15, and the venting of the other of the nosepieces 21, 23 to atmosphere. In this embodiment the valves 35, 37 are electrically-operated valves.

Each of the valves 35, 37 comprises a first port which is fluidly connected to the respective nosepiece 21, 23, a second port which is fluidly connected to the respective substance supply unit 13, 15, a third port which is fluidly connected to the gas supply

channel 33, and a fourth port which vents to atmosphere. Each of the valves 35, 37 is operable between a first, delivery position in which the first, second and third ports thereof are open and the fourth port thereof is closed, whereby substance can be delivered by the respective substance supply unit 13, 15 and entrained by the exhalation breath of a subject, and a second, venting position in which the first, second and fourth ports thereof are open and the third port thereof is closed, whereby the exhalation breath of a subject which has been driven through the nasal airway 1 of the subject is vented to atmosphere.

The delivery device 11 further comprises first and second flow resistor units 39, 41 for providing a flow resistance to vented air flow which are fluidly connected to respective ones of the fourth ports of the valves 35, 37. In one embodiment the flow resistor units 39, 41 can each include a filter for preventing the escape of substance.

In this embodiment the flow resistor units 39, 41 each include a flow resistor of fixed flow resistance for providing a fixed flow resistance to vented air flow.

In another embodiment the flow resistor units 39, 41 could include a progressive flow resistor for providing a progressively increasing flow resistance to vented air flow. In one embodiment the flow resistor units 39, 41 could include an inflatable balloon. In one embodiment the flow resistor units 39, 41 could be configured to vent to atmosphere subsequent to the generation of a predetermined pressure, for example, a pressure which exceeds the opening pressure for the paranasal sinus ostia 5 and the tubal ostia 7. With this configuration, following the development of a pressure exceeding the opening pressure for the paranasal sinus ostia 5 and the tubal ostia 7, the flow resistance gradually decreases and the air flow increases. This pressure and flow regime can promote the deposition of airborne particles in the nasal airway 1. Furthermore, this pressure and flow regime ensures that airborne particles are flushed out of the nasal airway 1 before the procedure is terminated, thereby preventing airborne particles, which could subsequently be inhaled, from remaining in the nasal airway 1.

The delivery device 11 further comprises first and second flow meters 43, 45 which are disposed in respective ones of the flow channels 25, 27 of the first and second nosepiece

units 17, 19 for detecting the flow rate of the flow therethrough. In this embodiment the flow meters 43, 45 are disposed in the respective ones of the flow channels 25, 27 of the nosepiece units 17, 19 intermediate the respective nosepiece 21, 23 and the respective valve 35, 37.

The delivery device 11 further comprises first and second pressure sensors 47, 49 which are disposed in respective ones of the flow channels 25, 27 of the first and second nosepiece units 17, 19 for detecting the pressure therein. In this embodiment the pressure sensors 47, 49 are disposed in the respective ones of the flow channels 25, 27 of the nosepiece units 17, 19 intermediate the respective nosepiece 21, 23 and the respective valve 35, 37.

The delivery device 11 further comprises a control unit 51 for controlling the operation thereof. The control unit 51 is operably connected to the first and second substance supply units 13, 15, the first and second valves 35, 37 of the valve unit, the first and second flow meters 43, 45, and the first and second pressure sensors 47, 49, whereby the first and second substance supply units 13, 15 can be actuated in response to one or both of detected pressures and flow rates.

Operation of the delivery device 11 will now be described hereinbelow.

Firstly, as illustrated in Figure 2(a), the nosepieces 21, 23 of the nosepiece units 17, 19 are fitted to the respective nostrils of a subject and the mouthpiece 31 is gripped in the lips of the subject. With this configuration, the delivery device 11 provides for three-point fixation, and thereby ensures reliable repeated delivery to the nasal cavities 2, 3 of a subject.

When first taking the delivery device 11, one of the valves 35, 37 of the valve unit, in this embodiment the first valve 35, is in the delivery position such that the gas supply channel 33 and the respective substance supply unit 13 are in fluid communication with the respective nosepiece 21, and the other of the valves 35, 37 of the valve unit, in this embodiment the second valve 37, is in the venting position such as to vent the other nosepiece 23.

As illustrated in Figure 2(b), the subject then begins to exhale through the mouthpiece 31, which exhalation acts to close the oropharyngeal velum of the subject and increase the pressure in the nasal airway 1 by the introduction of exhaled air from the exhalation breath thereinto, with the second flow resistor unit 41 providing a flow resistance to the exhaled air flow.

In one mode of operation, the delivery device 11 is configured to be actuated on the generation of a predetermined actuation pressure. In one embodiment the first pressure sensor 43 is utilized to detect the actuation pressure. In another embodiment the second pressure sensor 45 is utilized to detect the actuation pressure. On detection of the actuation pressure, the control unit 51 acts to actuate the first substance supply unit 13 to supply a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

In another mode of operation, the delivery device 11 is configured to be actuated on the generation of a predetermined flow rate. In one embodiment the first flow meter 47 is utilized to detect the actuation flow rate. In another embodiment the second flow meter 49 is utilized to detect the actuation flow rate. On detection of the actuation flow rate, the control unit 51 acts to actuate the first substance supply unit 13 to deliver a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

Following actuation of the first substance supply unit 13, as illustrated in Figure 2(c), the valve unit is then re-configured by the control unit 51 such that the first valve 35 is moved to the venting position to vent the nosepiece 21 of the first nosepiece unit 17, and the second valve 37 is moved to the delivery position such that the gas supply channel 33 and the second substance supply unit 15 are in fluid communication with the nosepiece 23 of the second nosepiece unit 19.

In one mode of operation, the valve unit is re-configured on detection of a predetermined re-configuration pressure. In one embodiment the first pressure sensor 43 is utilized to detect the re-configuration pressure. In another embodiment the second pressure sensor 45 is utilized to detect the re-configuration pressure. On detection of the re-

configuration pressure, the control unit 51 acts to actuate the second substance supply unit 15 to supply a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

In another mode of operation, the delivery device 11 is configured to be actuated on the detection of a predetermined re-configuration flow volume. In one embodiment the first flow meter 47 is utilized to detect the re-configuration flow volume. In another embodiment the second flow meter 49 is utilized to detect the re-configuration flow volume. On detection of the re-configuration flow volume, the control unit 51 acts to actuate the second substance supply unit 15 to deliver a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

In a further mode of operation, the delivery device 11 is configured to be actuated on the elapse of a predetermined period of time following the actuation of the first substance supply unit 13. On the elapse of the predetermined period of time, the control unit 51 acts to actuate the second substance supply unit 15 to deliver a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

Following actuation of the second substance supply unit 15, the valve unit is then re-configured to the original configuration by the control unit 51 such that the first valve 35 is moved to the delivery position in which the gas supply channel 33 and the first substance supply unit 13 are in fluid communication with the nosepiece 21 of the first nosepiece unit 17, and the second valve 37 is moved to the venting position such as to vent the nosepiece 23 of the second nosepiece unit 19.

In one mode of operation, the valve unit is re-configured on detection of a predetermined re-configuration pressure. In one embodiment the first pressure sensor 43 is utilized to detect the re-configuration pressure. In another embodiment the second pressure sensor 45 is utilized to detect the re-configuration pressure.

In another mode of operation, the valve unit is re-configured on detection of a predetermined re-configuration flow volume. In one embodiment the first flow meter 47

is utilized to detect the re-configuration flow volume. In another embodiment the second flow meter 49 is utilized to detect the re-configuration flow volume.

In a further mode of operation, the valve unit is re-configured on the elapse of a predetermined period of time following the actuation of the second substance supply unit 15.

In this way, the delivery device 11 provides for the successive delivery of substance through each of the nostrils of the subject, which delivery is advantageous, both in terms of compliance and, particularly, in delivering substance to targeted posterior regions of the nasal airway 1.

In another embodiment the delivery device 11 could be configured such that the valve unit is re-configured more than twice in each operation, such as to provide for the repeated delivery of substance to alternate ones of the nostrils of the subject in each operation of the delivery device 11.

Figures 3(a) to (c) illustrate a nasal delivery device 11 in accordance with a second embodiment of the present invention.

The delivery device 11 of this embodiment is very similar to the delivery device 11 of the above-described first embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts.

The delivery device 11 of this embodiment differs from that of the above-described first embodiment in further comprising an exhalation breath actuatable gas supply unit 53 which is fluidly connected to the gas supply channel 33 for delivering a gas flow thereto and operably connected to the control unit 51, and in that the mouthpiece 31 is in fluid communication with the gas supply unit 53 and not the gas supply channel 33, whereby a gas flow is delivered by the gas supply unit 53 in response to exhalation by a subject into the mouthpiece 31.

The gas supply unit 53 includes a trigger mechanism 55 for actuating the same in response to exhalation by the subject, with the trigger mechanism 55 being operably coupled to the mouthpiece 31 such as to be actuated by the exhalation breath of the subject. In this embodiment the trigger mechanism 55 comprises a pressure sensor for actuating the gas supply unit 53 in response to the detection of a predetermined actuation pressure. In another embodiment the trigger mechanism 55 could comprise a flow meter for actuating the gas supply unit 53 in response to the detection of a predetermined flow rate.

In this embodiment the mouthpiece 31 includes a diaphragm which is acted upon by the exhalation breath of the subject to actuate the trigger mechanism 55 on the generation of the predetermined actuation pressure. With this configuration, where the mouthpiece 31 is disposable, no part of the delivery device 11, other than the disposable mouthpiece 31, is exposed to the exhalation breath of the subject, and the delivery device 11 can be used to deliver substance to many subjects, such as in mass immunization or mass vaccination, without the risk of cross-contamination.

Operation of the delivery device 11 is the same as for the above-described first embodiment, with a gas flow being provided by the gas supply unit 53 instead of being developed by the exhalation breath of the subject.

In one embodiment the gas supply unit 53 is configured to deliver a gas flow at such a flow rate as to develop a predetermined pressure in the nasal airway 1.

In another embodiment the gas supply unit 53 could be configured to deliver a gas flow which has an alternating flow and is such as to develop an alternating pressure within the nasal airway 1. By cycling the pressure within the nasal airway 1, improved delivery of substance to the paranasal sinuses 6 and the tuba auditiva 8 and the middle ears 9 can be achieved. In one embodiment the delivery device 11 can be configured to provide for delivery of substance through only one nostril of the subject.

In a further embodiment, at least one of the first and second flow resistors 39, 41 could comprise an expandable chamber, such as an inflatable balloon, and the gas supply unit

53 could be configured alternately to deliver and withdraw a volume of gas through the nasal airway 1 from either one or alternately both of the nostrils of the subject, which delivery and withdrawal would be such as to cause a volume of gas which entrains substance to be flushed repeatedly through the nasal airway 1 in opposite directions. Repeatedly flushing a volume of gas entraining substance in alternate directions through the nasal airway 1 would provide for improved delivery of substance. In one embodiment the delivery device 11 can be configured to provide for delivery of substance through only one nostril of the subject.

Figures 4(a) to (c) illustrate a nasal delivery device 111 in accordance with a third embodiment of the present invention.

The delivery device 111 comprises a substance supply unit 113 for supplying a metered dose of substance. In preferred embodiments the substance comprises a medicament, especially systemic or topical pharmaceuticals, or a vaccine.

In this embodiment the substance supply unit 113 comprises a nebulizer which delivers a metered dose of substance, here continuously as an aerosol spray, on actuation thereof.

The delivery device 111 further comprises first and second nosepiece units 117, 119 for fitting to respective ones of the nostrils of a subject. In this embodiment the nosepiece units 117, 119 each comprise a nosepiece 121, 123 for fitting to respective ones of the nostrils of a subject and a flow channel 125, 127 which fluidly connects the respective one of the nosepieces 121, 123 to the substance supply unit 113. In this embodiment the nosepieces 121, 123 are replaceable elements.

The delivery device 111 further comprises a mouthpiece 131 which is gripped by the lips of a subject and through which the subject exhales. In this embodiment the mouthpiece 131 is a replaceable element. In a preferred embodiment the nosepieces 121, 123 and the mouthpiece 131 are integrally formed as a single element such as to allow for replacement after use. In this way, the delivery device 111 can be used with many different subjects, for example, in mass immunization or mass vaccination, and yet avoid the possibility of cross-contamination from subject to subject.

The delivery device 111 further comprises a gas supply channel 133 which fluidly connects the substance supply unit 113 and the mouthpiece 131.

The delivery device 111 further comprises a valve unit which comprises first and second valves 135, 137 which are disposed in respective ones of the flow channels 125, 127 of the first and second nosepiece units 117, 119 such as to provide for the selective communication of one of the nosepieces 121, 123 with the substance supply unit 113 and mouthpiece 131, and the venting of the other of the nosepieces 121, 123 to atmosphere. In this embodiment the valves 135, 137 are electrically-operated valves.

Each of the valves 135, 137 comprises a first port which is fluidly connected to the respective nosepiece 121, 123, a second port which is fluidly connected to the substance supply unit 113, and a third port which vents to atmosphere. Each of the valves 135, 137 is operable between a first, delivery position in which the first and second ports thereof are open and the third port thereof is closed, whereby substance can be delivered by the substance supply unit 113 and entrained by the exhalation breath of a subject, and a second, venting position in which the first and third ports thereof are open and the second port thereof is closed, whereby the exhalation breath of a subject which has been driven through the nasal airway 1 of the subject is vented to atmosphere.

The delivery device 111 further comprises first and second flow resistor units 139, 141 for providing a flow resistance to vented air flow which are fluidly connected to respective ones of the third ports of the valves 135, 137. In one embodiment the flow resistor units 139, 141 can each include a filter for preventing the escape of substance.

In this embodiment the flow resistor units 139, 141 each include a flow resistor of fixed flow resistance for providing a fixed flow resistance to vented air flow.

In another embodiment the flow resistor units 139, 141 could include a progressive flow resistor for providing a progressively increasing flow resistance to vented air flow. In one embodiment the flow resistor units 139, 141 could include an inflatable balloon. In one embodiment the flow resistor units 139, 141 could be configured to vent to

atmosphere subsequent to the generation of a predetermined pressure, for example, a pressure which exceeds the opening pressure for the paranasal sinus ostia 5 and the tubal ostia 7. With this configuration, following the development of a pressure exceeding the opening pressure for the paranasal sinus ostia 5 and the tubal ostia 7, the flow resistance gradually decreases and the air flow increases. This pressure and flow regime can promote the deposition of airborne particles in the nasal airway 1. Furthermore, this pressure and flow regime ensures that airborne particles are flushed out of the nasal airway 1 before the procedure is terminated, thereby preventing airborne particles, which could subsequently be inhaled, from remaining in the nasal airway 1.

The delivery device 111 further comprises first and second flow meters 143, 145 which are disposed in respective ones of the flow channels 125, 127 of the first and second nosepiece units 117, 119 for detecting the flow rate of the flow therethrough. In this embodiment the flow meters 143, 145 are disposed in the respective ones of the flow channels 125, 127 of the nosepiece units 117, 119 intermediate the respective nosepiece 121, 123 and the respective valve 135, 137.

The delivery device 111 further comprises first and second pressure sensors 147, 149 which are disposed in respective ones of the flow channels 125, 127 of the first and second nosepiece units 117, 119 for detecting the pressure therein. In this embodiment the pressure sensors 147, 149 are disposed in the respective ones of the flow channels 125, 127 of the nosepiece units 117, 119 intermediate the respective nosepiece 121, 123 and the respective valve 135, 137.

The delivery device 111 further comprises a control unit 151 for controlling the operation thereof. The control unit 151 is operably connected to the substance supply unit 113, the first and second valves 135, 137 of the valve unit, the first and second flow meters 143, 145, and the first and second pressure sensors 147, 149, whereby the substance supply unit 113 can be actuated in response to one or both of detected pressures and flow rates.

Operation of the delivery device 111 will now be described hereinbelow.

Firstly, as illustrated in Figure 4(a), the nosepieces 121, 123 of the nosepiece units 117, 119 are fitted to the respective nostrils of a subject and the mouthpiece 131 is gripped in the lips of the subject. With this configuration, the delivery device 111 provides for three-point fixation, and thereby ensures reliable repeated delivery to the nasal cavities 2, 3 of a subject.

When first taking the delivery device 111, one of the valves 135, 137 of the valve unit, in this embodiment the first valve 135, is in the delivery position such that the substance supply unit 113 is in fluid communication with the nosepiece 121 of the first nosepiece unit 117, and the other of the valves 135, 137 of the valve unit, in this embodiment the second valve 137, is in the venting position such as to vent the nosepiece 123 of the second nosepiece unit 119.

As illustrated in Figure 4(b), the subject then begins to exhale through the mouthpiece 131, which exhalation acts to close the oropharyngeal velum of the subject and increase the pressure in the nasal airway 1 by the introduction of exhaled air from the exhalation breath thereinto, with the second flow resistor unit 141 providing a flow resistance to the exhaled air flow.

In one mode of operation, the delivery device 111 is configured to be actuated on the generation of a predetermined actuation pressure. In one embodiment the first pressure sensor 143 is utilized to detect the actuation pressure. In another embodiment the second pressure sensor 145 is utilized to detect the actuation pressure. On detection of the actuation pressure, the control unit 151 acts to actuate the substance supply unit 113 to commence delivery of a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

In another mode of operation, the delivery device 111 is configured to be actuated on the generation of a predetermined flow rate. In one embodiment the first flow meter 147 is utilized to detect the actuation flow rate. In another embodiment the second flow meter 149 is utilized to detect the actuation flow rate. On detection of the actuation flow rate, the control unit 151 acts to actuate the substance supply unit 113 to commence delivery

of a metered dose of substance, which substance is entrained by the exhalation breath of the subject.

Following actuation of the substance supply unit 113, the valve unit remains in the one configuration for a predetermined period of time, in this embodiment for half of the time period required for the delivery of a predetermined metered dose of substance by the substance supply unit 113.

Following the elapse of the predetermined period of time, as illustrated in Figure 4(c), the valve unit is then re-configured by the control unit 151 such that the first valve 135 is moved to the venting position to vent the nosepiece 121 of the first nosepiece unit 117, and the second valve 137 is moved to the delivery position such that the substance supply unit 113 is in fluid communication with the nosepiece 123 of the second nosepiece unit 119.

In this way, the delivery device 111 provides for the successive delivery of substance through each of the nostrils of the subject, which delivery is advantageous, both in terms of compliance and, particularly, in delivering substance to targeted posterior regions of the nasal airway 1.

In another embodiment the delivery device 111 could be configured such that the valve unit is re-configured more than twice in each operation, such as to provide for the repeated delivery of substance to alternate ones of the nostrils of the subject in each operation of the delivery device 111. In this embodiment this repeated alternation of the delivery nostril is achieved by directing the exhalation breath of a subject to alternate ones of the nostrils of the subject.

In alternative embodiments the substance supply unit 113 could comprise an aerosol canister for delivering a metered volume of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing substance, either as a suspension or solution, a mechanical delivery pump, in particular a liquid delivery pump or a powder delivery pump, which delivers a metered dose of substance on actuation thereof, or a dry powder delivery unit which delivers a metered dose of substance, as a dry powder, on actuation

thereof. These substance supply units 113 are primed, in one embodiment by loading a biasing element, and include a release mechanism, in this embodiment electrically-operated, which, when triggered, releases the biasing element and actuates the substance supply unit 113 to deliver a metered dose of substance. In such embodiments the substance supply unit 113 can be actuated for each alternation of the valve unit.

Figures 5(a) to (c) illustrate a nasal delivery device 111 in accordance with a fourth embodiment of the present invention.

The delivery device 111 of this embodiment is very similar to the delivery device 111 of the above-described third embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts

The delivery device 111 of this embodiment differs from that of the above-described third embodiment in further comprising an exhalation breath actuatable gas supply unit 153 which is fluidly connected to the gas supply channel 133 for delivering a gas flow thereto and operably connected to the control unit 151, and in that the mouthpiece 131 is in fluid communication with the gas supply unit 153 and not the gas supply channel 133, whereby a gas flow is delivered by the gas supply unit 153 in response to exhalation through the mouthpiece 131.

The gas supply unit 153 includes a trigger mechanism 155 for actuating the same in response to exhalation by the subject, with the trigger mechanism 155 being operably coupled to the mouthpiece 131 such as to be actuated by the exhalation breath of the subject. In this embodiment the trigger mechanism 155 comprises a pressure sensor for actuating the gas supply unit 153 in response to the detection of a predetermined actuation pressure. In another embodiment the trigger mechanism 155 could comprise a flow meter for actuating the gas supply unit 153 in response to the detection of a predetermined flow rate.

In this embodiment the mouthpiece 131 includes a diaphragm which is acted upon by the exhalation breath of the subject to actuate the trigger mechanism 155 on the generation

of the predetermined actuation pressure. With this configuration, where the mouthpiece 131 is disposable, no part of the delivery device 111, other than the disposable mouthpiece 131, is exposed to the exhalation breath of the subject, and the delivery device 111 can be used to deliver substance to many subjects, such as in mass immunization or mass vaccination, without the risk of cross-contamination.

Operation of the delivery device 111 is the same as for the above-described third embodiment, with a gas flow being provided by the gas supply unit 153 instead of being developed by the exhalation breath of the subject.

In one embodiment the gas supply unit 153 is configured to deliver a gas flow at such a flow rate as to develop a predetermined pressure in the nasal airway 1.

In another embodiment the gas supply unit 153 could be configured to deliver a gas flow which has an alternating flow and is such as to develop an alternating pressure within the nasal airway 1. By cycling the pressure within the nasal airway 1, improved delivery of substance to the paranasal sinuses 6 and the tuba auditiva 8 and the middle ears 9 can be achieved. In one embodiment the delivery device 111 can be configured to provide for delivery of substance through only one nostril of the subject.

In a further embodiment, at least one of the first and second flow resistors 139, 141 could comprise an expandable chamber, such as an inflatable balloon, and the gas supply unit 153 could be configured alternately to deliver and withdraw a volume of gas through the nasal airway 1 from either one or alternately both of the nostrils of the subject, which delivery and withdrawal would be such as to cause a volume of gas which entrains substance to be flushed repeatedly through the nasal airway 1 in opposite directions. Repeatedly flushing a volume of gas entraining substance in alternate directions through the nasal airway 1 would provide for improved delivery of substance. In one embodiment the delivery device 111 can be configured to provide for delivery of substance through only one nostril of the subject.

Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined by the appended claims.

In the described embodiments the mouthpieces 31, 131 are configured to be gripped in the lips of a subject. In alternative embodiments the mouthpieces 31, 131 could be configured to be gripped by the teeth of a subject and sealed by the lips of the subject. In preferred embodiments the mouthpieces 31, 131 could be specifically configured to have one or both of a shape or geometry which allows the delivery devices to be gripped repeatedly in the same position, thereby providing for the respective nosepieces 21, 23, 121, 123 to be reliably inserted in the same position in the nasal cavities 2, 3.

In preferred embodiments the delivery devices 11, 111 are configured to deliver substance through one nostril of a subject at such a pressure as to flow around the posterior margin of the nasal septum 4 and out of the other nostril of the subject, thereby achieving bi-directional delivery through the nasal cavities 2, 3 as disclosed in WO-A-00/51672. In alternative embodiments the delivery devices 11, 111 can be configured to deliver substance at a reduced pressure which is not sufficient to achieve bi-directional delivery through the nasal cavities 2, 3.

CLAIMS

1. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
first and second nosepiece units, each including a nosepiece for fitting to respective nostrils of a subject;
at least one substance supply unit for supplying substance for delivery to the nasal airway of the subject; and
a valve unit for selectively fluidly connecting the at least one substance supply unit alternately to respective ones of the nosepiece units.

2. The delivery device of claim 1, further comprising:
a mouthpiece through which the subject in use exhales.

3. The delivery device of claim 1 or 2, further comprising:
a gas supply channel for supplying a gas flow for entraining substance supplied by the at least one substance supply unit.

4. The delivery device of claim 3 when appendant upon claim 2, wherein the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

5. The delivery device of claim 3, further comprising:
a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

6. The delivery device of claim 5 when appendant upon claim 2, wherein the gas supply unit is an exhalation breath actuatable unit which is fluidly connected to the mouthpiece such as to be actuated on exhalation by the subject.

7. The delivery device of any of claims 3 to 6, wherein the valve unit is configured alternately fluidly to connect one of the nosepiece units to the at least one substance supply unit and vent the other of the nosepiece units, such that, where

the gas flow is at a driving pressure which is such as to cause the gas flow to flow around the posterior margin of the nasal septum and through the nasal airway, the gas flow delivered through the one nosepiece unit is vented through the other nosepiece unit.

8. The delivery device of claim 7, further comprising:
at least one flow resistor to which the other nosepiece unit is vented.

9. The delivery device of claim 8, wherein the flow resistor has a fixed flow resistance for providing a fixed flow resistance to the gas flow.

10. The delivery device of claim 8, wherein the flow resistor is a progressive resistor for progressively providing an increasing flow resistance to the gas flow.

11. The delivery device of claim 10, wherein the progressive resistor comprises an expandable member which provides a progressively increasing resistance to the gas flow.

12. The delivery device of any of claims 1 to 11, further comprising:
a control unit for controlling the valve unit such as to provide for alternate delivery of substance through respective ones of the first and second nosepiece units.

13. The delivery device of any of claims 1 to 12, comprising:
a single substance supply unit for supplying substance for delivery alternately to respective ones of the first and second nosepiece units.

14. The delivery device of any of claims 1 to 12, comprising:
first and second substance supply units for supplying substance for delivery to respective ones of the first and second nosepiece units.

15. The delivery device of any of claims 1 to 14, wherein the valve unit comprises first and second valves, each being fluidly connected to a respective one of the first and second nosepiece units.

16. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
fitting first and second nosepiece units to respective nostrils of a subject; and
delivering substance alternately through respective ones of the nosepiece units.

17. The method of claim 16, further comprising the step of:
exhaling through a mouthpiece during delivery of substance.

18. The method of claim 17, wherein substance is delivered in a gas flow.

19. The method of claim 18, wherein the gas flow is an air flow developed by an exhalation breath of the subject.

20. The method of claim 18, wherein the gas flow is a gas flow separate to an exhalation breath of the subject.

21. The method of any of claims 18 to 20, wherein substance is delivered alternately to the nosepiece units and the other of the nosepiece units is vented, such that, where the gas flow is at a driving pressure which is such as to cause the gas flow to flow around the posterior margin of the nasal septum and through the nasal airway, the gas flow delivered through the one nosepiece unit is vented through the other nosepiece unit.

22. The method of claim 21, wherein the gas flow is vented through a flow resistor.

23. The method of claim 22, wherein the flow resistor has a fixed flow resistance and provides a fixed flow resistance to the gas flow.

24. The method of claim 22, wherein the flow resistor is a progressive resistor which provides a progressively increasing flow resistance to the gas flow.

25. The method of claim 24, wherein the progressive resistor comprises an expandable member which provides a progressively increasing resistance to the gas flow.

26. The method of any of claims 16 to 25, wherein substance is supplied from a single substance supply unit.

27. The method of any of claims 16 to 25, wherein substance is supplied to the first and second nosepiece units from respective ones of first and second substance supply units.

28. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
at least one delivery unit for delivering substance to a nasal airway of a subject; and
a gas supply unit for applying a varying pressure in the nasal airway of the subject.

29. The delivery device of claim 28, wherein the gas supply unit is configured to cycle the pressure in the nasal airway of the subject.

30. The delivery device of claim 29, wherein the gas supply unit is configured to provide an alternating pressure in the nasal airway of the subject.

31. The delivery device of any of claims 28 to 30, further comprising:
a mouthpiece through which the subject in use exhales.

32. The delivery device of claim 31, wherein the gas supply unit is an exhalation breath actuatable unit which is fluidly connected to the mouthpiece such as to be actuated on exhalation by the subject.

33. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
delivering substance to a nasal airway of a subject; and
applying a varying pressure in the nasal airway of the subject.

34. The method of claim 33, wherein the step of applying a varying pressure in the nasal airway of the subject comprises the step of:
cycling the pressure in the nasal airway of the subject.

35. The method of claim 34, wherein the step of applying a varying pressure in the nasal airway of the subject comprises the step of:
alternating the pressure in the nasal airway of the subject.

36. The method of any of claims 33 to 35, further comprising the step of:
exhaling through a mouthpiece during delivery of substance.

37. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
at least one delivery unit for delivering substance to a nasal airway of a subject; and
a gas supply unit for alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

38. The delivery device of claim 37, further comprising:
a mouthpiece through which the subject in use exhales.

39. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
delivering substance to a nasal airway of a subject; and

alternately delivering and withdrawing a volume of gas through the nasal airway of the subject such as to cause entrained substance to be flushed in alternate directions therethrough.

40. The method of claim 39, further comprising the step of:
exhaling through a mouthpiece during delivery of substance.

41. An interface member for attachment to a nasal delivery device, comprising, as an integral element, at least one nosepiece for fitting to a nostril of a subject and a mouthpiece through which the subject in use exhales.

42. The interface member of claim 41, comprising first and second nosepieces for fitting to respective nostrils of a subject.

43. The interface member of claim 41 or 42, where being a disposable element.

44. The interface member of any of claims 41 to 43, wherein the mouthpiece comprises a tubular section through which the subject in use exhales.

45. The interface member of any of claims 41 to 43, wherein the mouthpiece includes a flexible member which is deflectable on exhalation into the mouthpiece.

46. The interface member of claim 45, wherein the mouthpiece comprises a cavity into which the subject in use exhales, with a part of the cavity being defined by the flexible member.

47. The interface member of claim 45 or 46, wherein the flexible member comprises a resilient member.

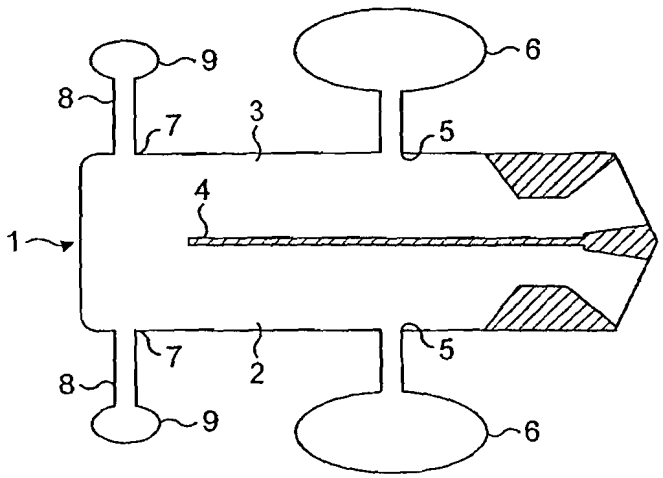

FIG. 1

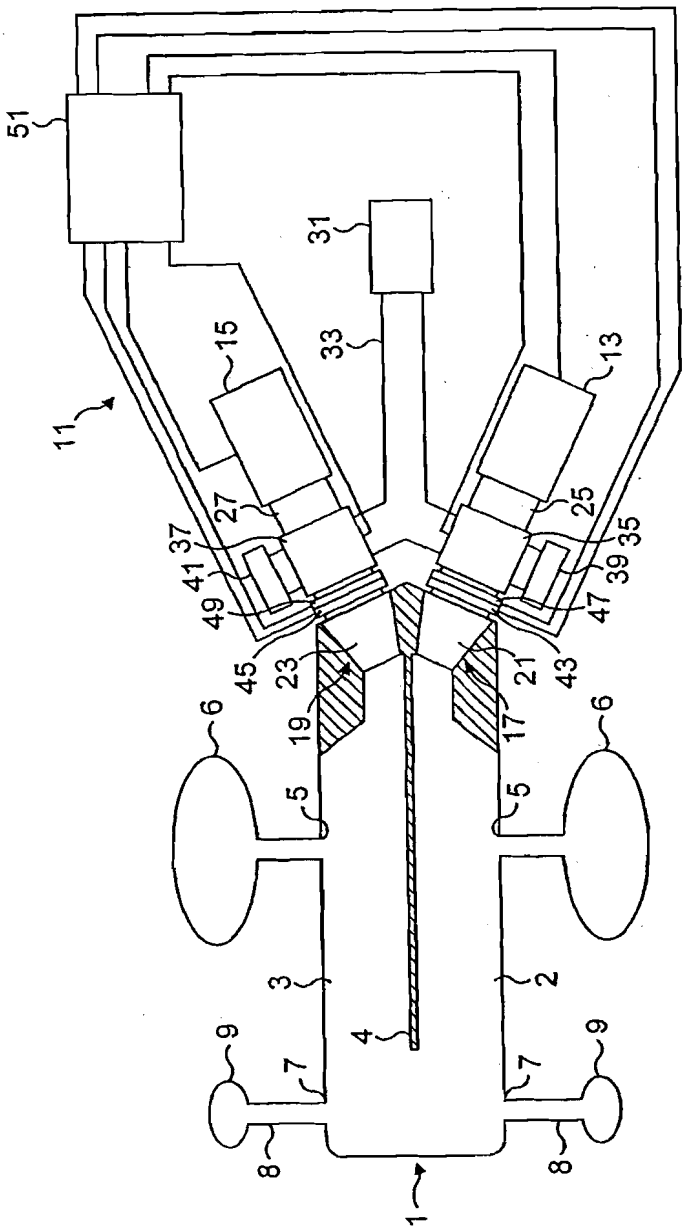
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FIG. 2(a)

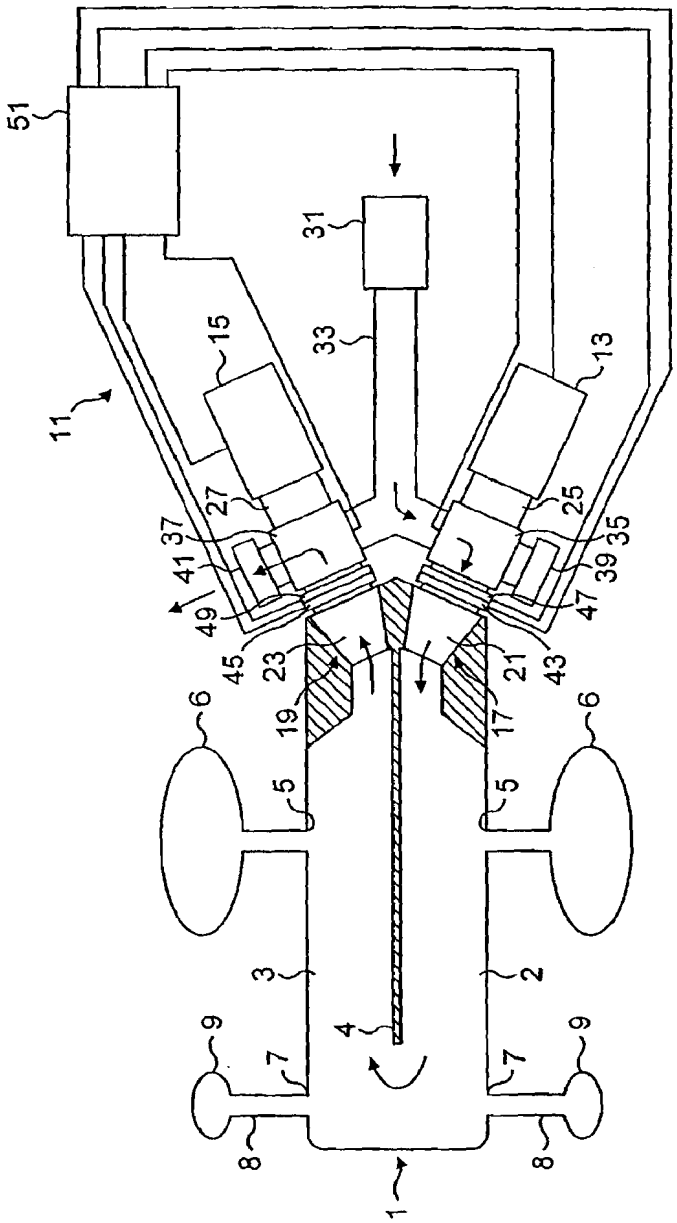
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FIG. 2(b)

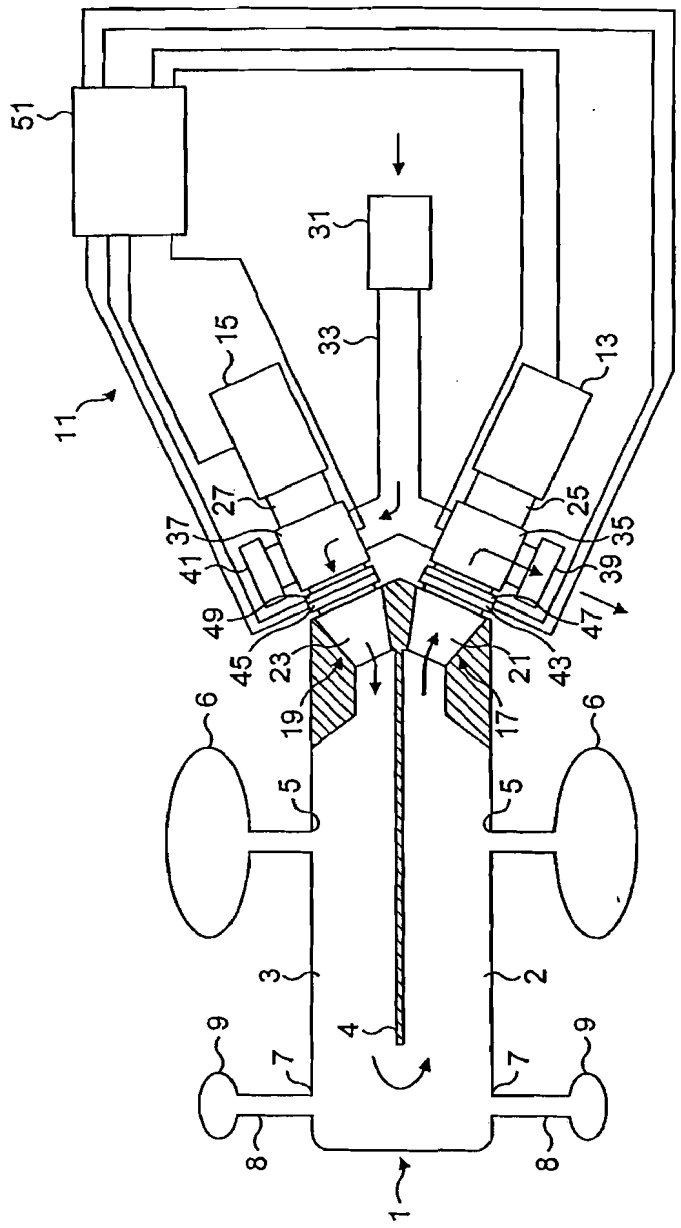
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FIG. 2(c)

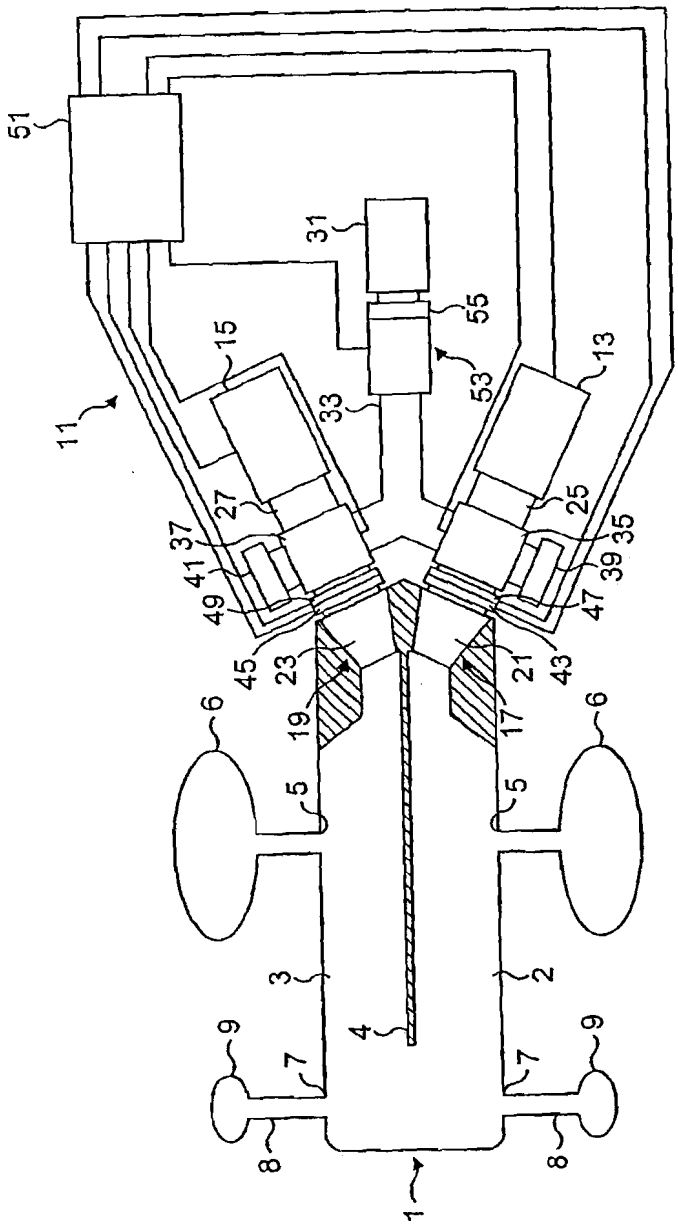
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FIG. 3(a)

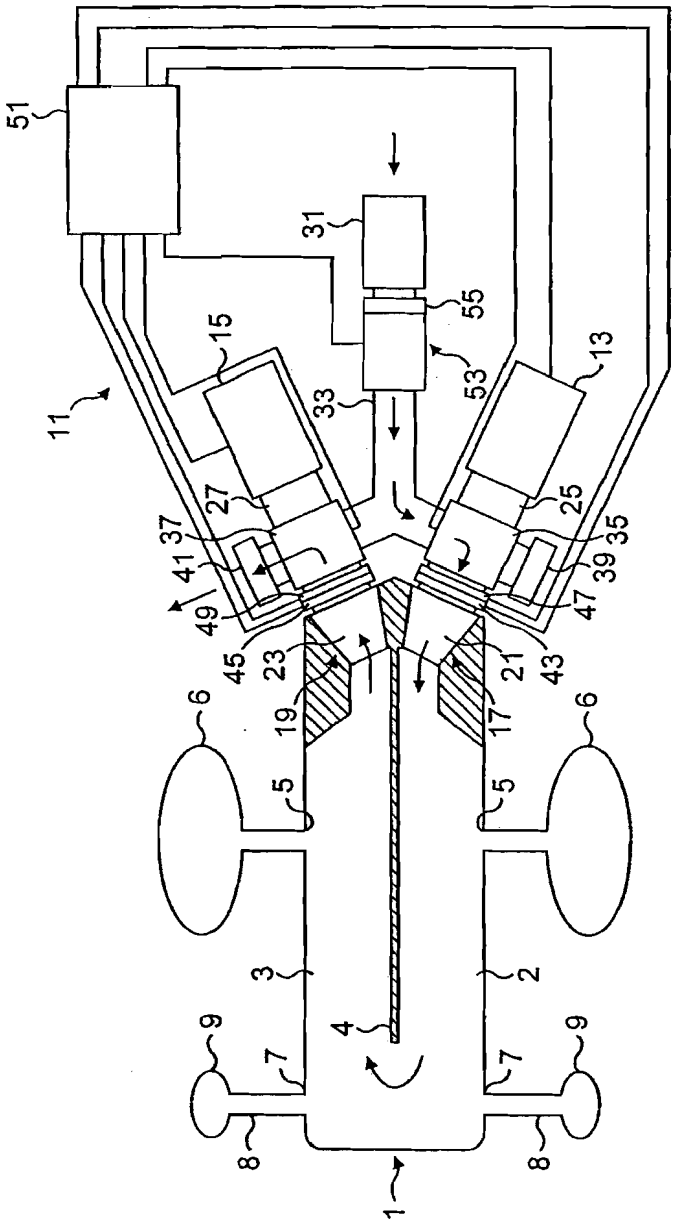
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FIG. 3(b)

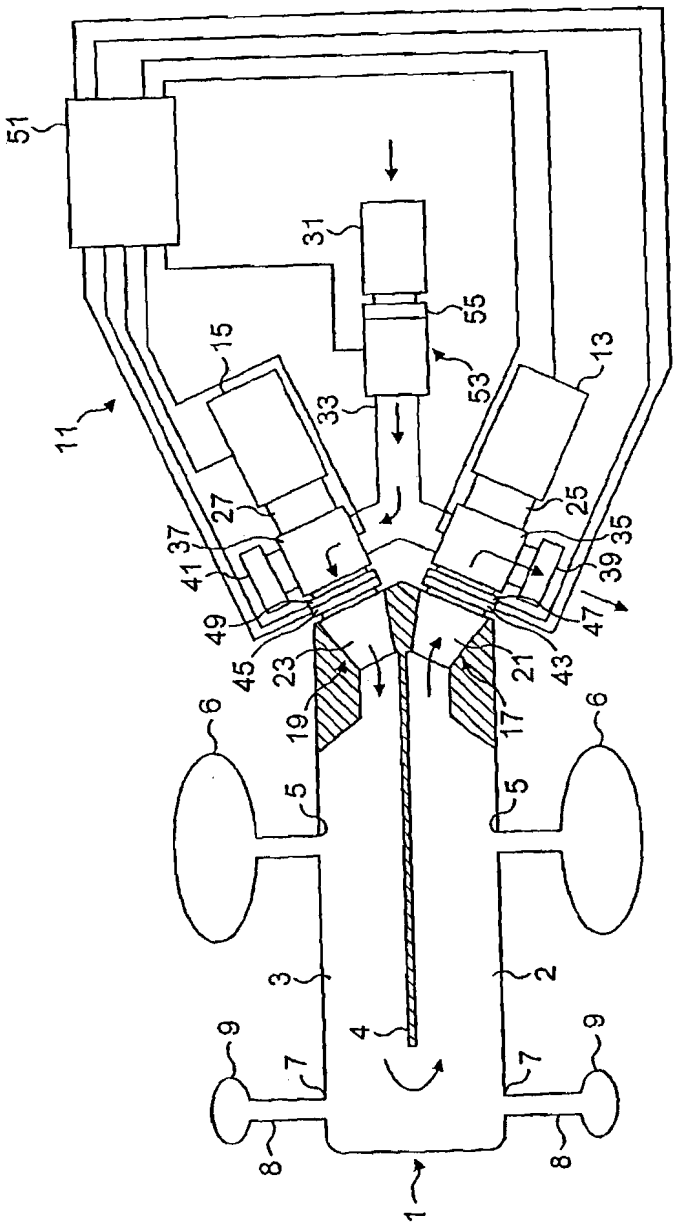
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FIG. 3(C)

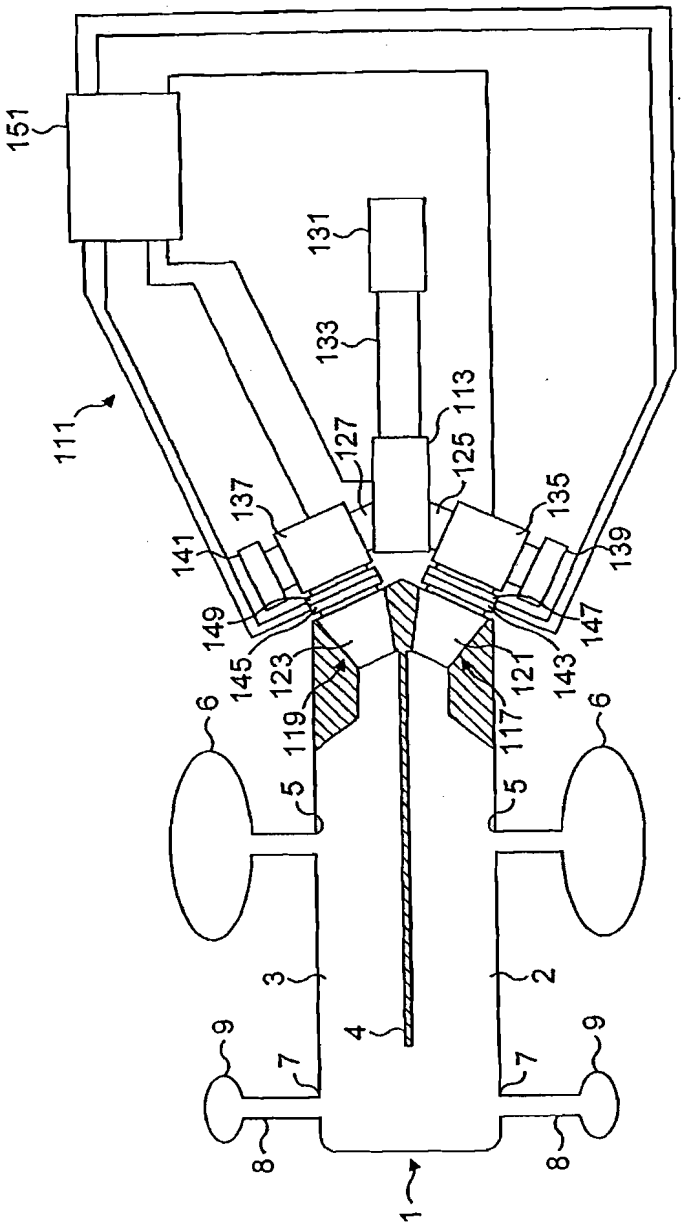
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FIG. 4(a)

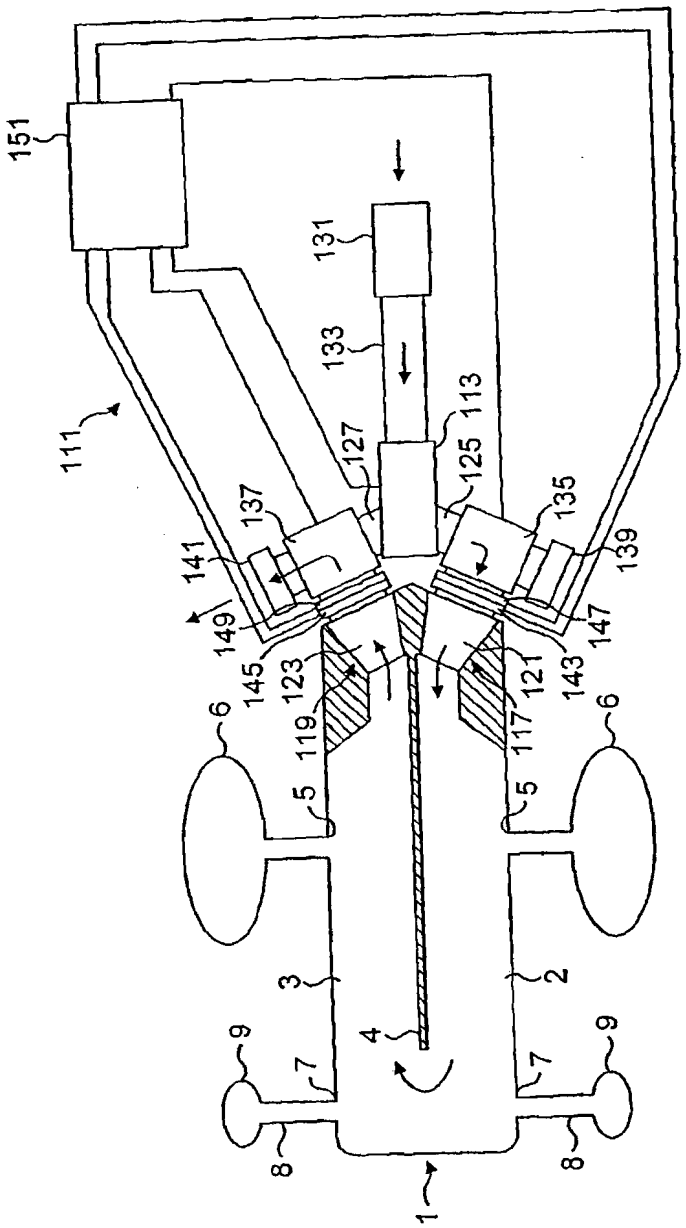
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FIG. 4(b)

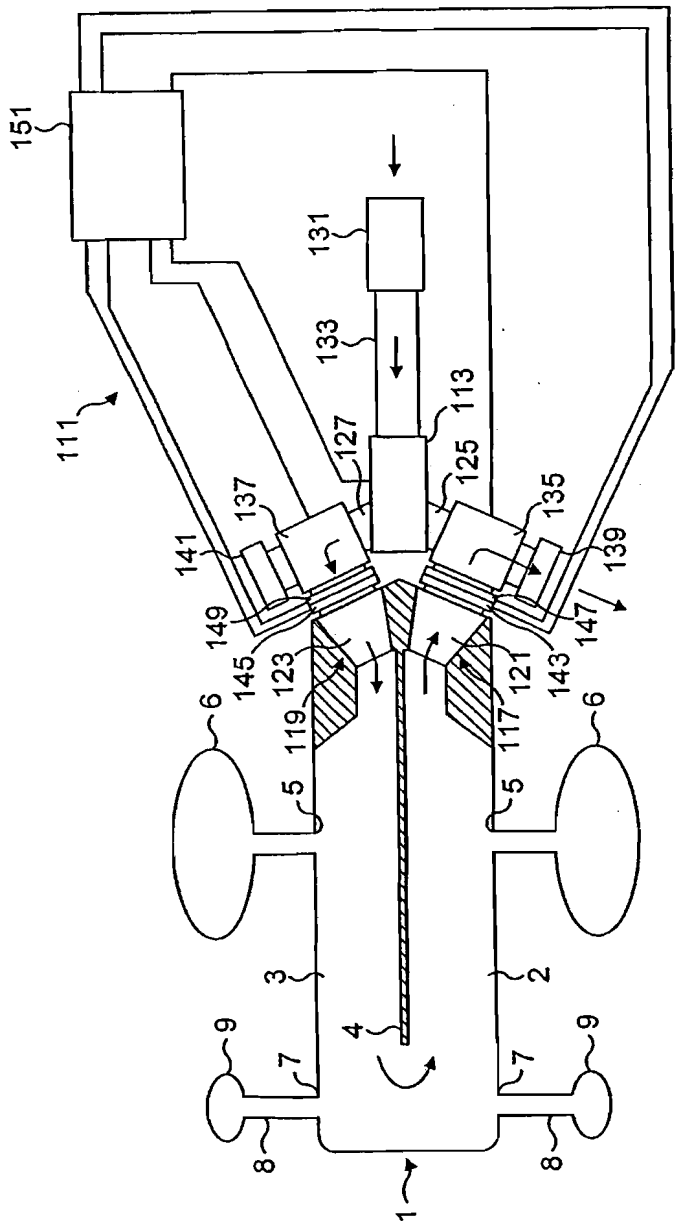
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FIG. 4(c)

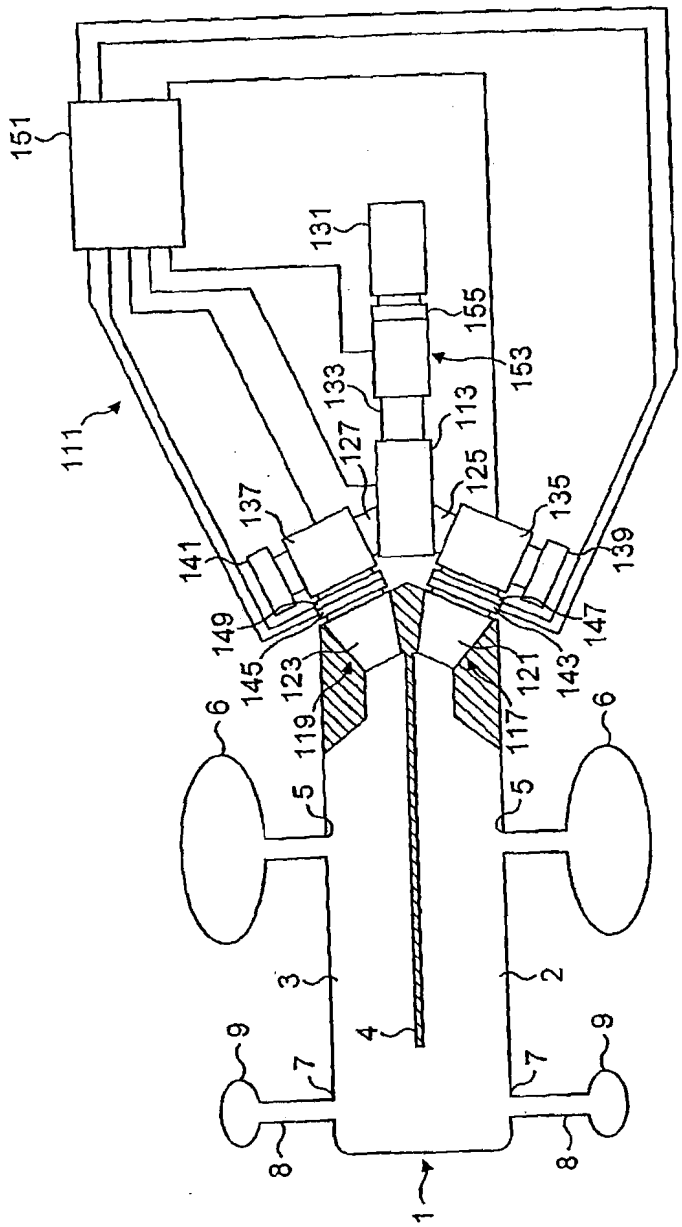
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FIG. 5(a)

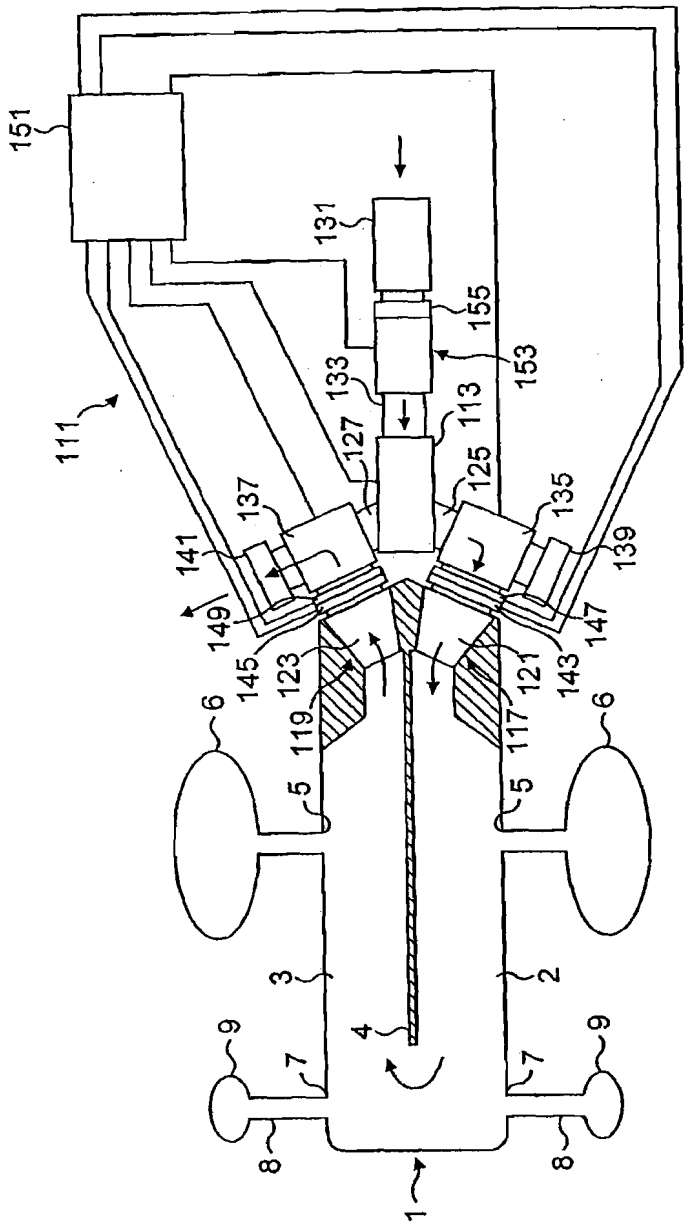
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FIG. 5(b)

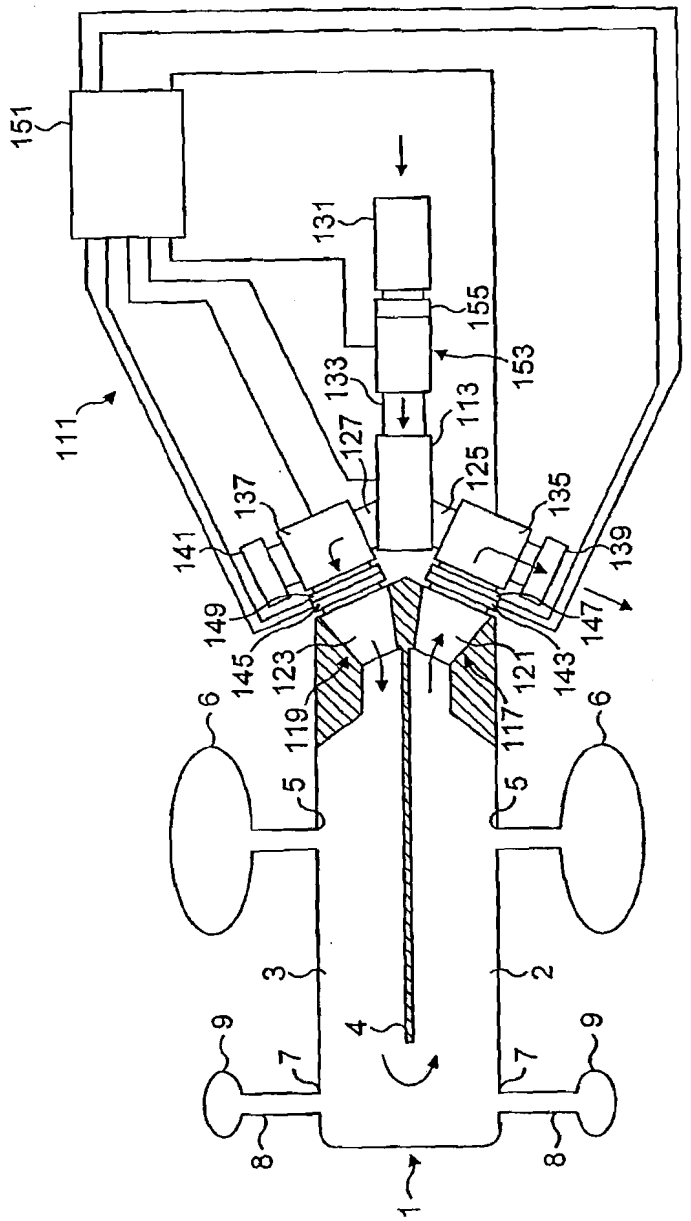
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FIG. 5(C)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/IB 03/01557

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M16/06 A61M15/08 A61M16/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 78818 A (TRUDELL MEDICAL INTERNAT) 25 October 2001 (2001-10-25)	1,3,5, 13,28
A	page 16, line 5 -page 17, line 24	15,37
A	WO 99 19013 A (VIRANYI PAUL) 22 April 1999 (1999-04-22) page 8, line 14 -page 9, line 8; figures 1,3	1
X	GB 408 856 A (HENRY FRANKEMOELLER; WIETSKE VAN SETERS BOSCH) 19 April 1934 (1934-04-19) page 1, right-hand column, line 93 -page 2, left-hand column, line 26; figure 1	1-6, 41-47
A	page 1, left-hand column, line 28 - line 30	28-32, 37,38

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 August 2003	14/08/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kroeders, M

INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/IB 03/01557

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 392 772 A (ZILBERSHTEIN MICHAEL) 28 February 1995 (1995-02-28) column 2, line 4 -column 3, line 14; figures 2A-4C	1
X	WO 00 51672 A (DJUPESLAND PER GISLE) 8 September 2000 (2000-09-08) cited in the application	28,31,32
A	page 17, line 16 -page 19, line 13	1-11,37, 38
X	US 5 271 391 A (GRAVES LINDA) 21 December 1993 (1993-12-21) column 3, line 46 -column 4, line 3; figure 1	28-30,37
X	US 5 099 836 A (LOESCHER THOMAS C ET AL) 31 March 1992 (1992-03-31)	28,29
A	column 4, line 60 -column 5, line 40; figures 1,8	32
X	US 2 566 806 A (MILLER HUGH A) 4 September 1951 (1951-09-04)	28,37
A	column 3, line 59 -column 5, line 19; figure 1	29,30
X	WO 98 53869 A (KELDMANN ERIK; KELDMANN TROELS (DK); DIRECT HALER A S (DK); PELAEZ) 3 December 1998 (1998-12-03)	41-47
A	page 10, line 34 -page 11, line 6; figure 4 page 12, line 28 -page 14, line 5; figures 11-13	1-6,13, 28-32, 37,38

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-15

A nasal delivery device comprising:
A) first and second nosepiece units
B) at least one substance supply unit
C) a valve unit
(selective supply of substance)

2. Claims: 28-32

A nasal delivery device comprising:
B) at least one delivery unit (= substance supply unit?)
D) a gas supply unit
(supplying gas flow)

3. Claims: 37, 38

A nasal delivery device comprising:
B) at least one delivery unit (= substance supply unit?)
E) a gas supply unit
(additionally extracting air)

4. Claims: 41-47

An interface member comprising:
A) at least one nosepiece
F) a mouthpiece
(providing exhalation triggering)

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IB 03/01557

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 16-27, 33-36, 39, 40
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/IB 03/01557

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			US	2002165482 A1	07-11-2002

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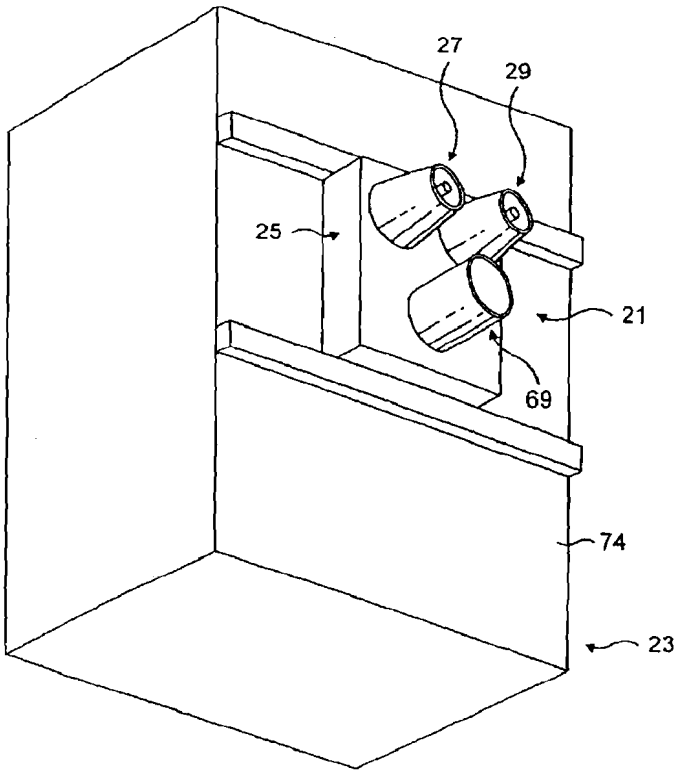
(54) Title: NASAL DEVICES



(57) Abstract: A nasal delivery device for and a method of delivering substance to a nasal airway of a subject, in particular in the mass treatment, especially mass vaccination, of subjects, the delivery device comprising: an interface unit, as a replaceable unit, including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit; and an actuation unit for actuating the at least one delivery unit of the interface unit.

WO 2004/004814 A2

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

NASAL DEVICES

The present invention relates to a nasal delivery device for and a method of delivering a substance, in particular one of a liquid, as a suspension or solution, or a powder containing a medicament, especially systemic or topical pharmaceuticals, or a vaccine to the nasal airway of a subject, in particular for the mass treatment, especially vaccination, of subjects.

Referring to Figure 1, the nasal airway 1 comprises the two nasal cavities separated by the nasal septum, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 3 and the tubal ostia 5, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx 7, the oral cavity 9 and the lower airway 11, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx 7 and the oral cavity 9 by opening and closing of the oropharyngeal velum 13. The velum 13, which is often referred to as the soft palate, is illustrated in solid line in the closed position, as achieved by providing a certain positive pressure in the oral cavity 9, such as achieved on exhalation through the oral cavity 9, and in dashed line in the open position.

There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such

as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitonin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa advantageously provides for rapid systemic uptake.

Nasal delivery also provides for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and also other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

Nasal delivery also further provides an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

Furthermore, nasal delivery also further provides for the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

Still furthermore, and a prime focus of the present invention is the nasal delivery of vaccines. The nasal delivery device of the present invention has been developed with the particular aim of providing a delivery device for the mass treatment, in particular the mass vaccination, of subjects.

For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse effects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

WO-A-00/51672 discloses a delivery device for delivering a substance, in particular a medicament, in a bi-directional flow through the nasal cavities, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril. This bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

It is an aim of the present invention to provide improved nasal delivery devices and nasal delivery methods for providing for the delivery of substance to subjects, in particular for the mass treatment, especially vaccination, of subjects.

In one aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: an interface unit, as a replaceable unit, including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit; and an actuation unit for actuating the at least one delivery unit of the interface unit.

Preferably, the interface unit comprises a disposable unit.

Preferably, the interface unit comprises a single integral unit.

Preferably, the interface unit is packaged in protective packaging.

In one embodiment the delivery device comprises: a plurality of interface units attached to a belt such as to allow for successive attachment of the interface units to the actuation unit.

Preferably, the actuation unit is configured successively to provide the interface units thereto through use of the belt as a guide.

Preferably, the substance supply unit comprises a substance pump unit for delivering substance, the substance pump unit including a chamber containing substance and a piston member which is movable in the chamber to deliver a flow of substance from the chamber.

In one embodiment the substance comprises a liquid.

In another embodiment the substance comprises a powder.

Preferably, the interface unit includes a mouthpiece unit including a mouthpiece into which a subject in use exhales.

In one embodiment the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by a subject into the mouthpiece.

In one embodiment the at least one delivery unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

Preferably, the gas supply unit comprises a gas pump unit for delivering a gas flow, the gas pump unit comprising a cylinder and a piston member which is movable in the cylinder to deliver a gas flow through the at least one nosepiece unit.

In one embodiment the at least one delivery unit is configured such that the gas supply unit initiates supply of a gas flow prior to actuation of the substance supply unit to deliver substance.

In another embodiment the actuation unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

In one embodiment the actuation unit is configured such that the gas supply unit initiates supply of a gas flow prior to actuation of the substance supply unit to deliver substance.

Preferably, the at least one delivery unit is actuated in response to exhalation by the subject.

In one embodiment the actuation unit includes a detection unit for detecting exhalation by a subject, at least one drive unit for actuating the at least one delivery unit, and a

control unit for actuating the at least one drive unit in response to detecting exhalation by the subject.

In one embodiment the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable pressure by the detection unit.

In another embodiment the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate by the detection unit.

In another embodiment the actuation unit includes at least one drive unit for actuating the at least one delivery unit, and a trigger mechanism for actuating the at least one drive unit in response to exhalation by the subject.

In one embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

In another embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

Preferably, the interface unit includes first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each including a substance supply unit for delivering substance through the respective nosepiece unit.

More preferably, the actuation unit is configured to actuate the first and second delivery units in succession such that substance is first delivered into one nasal cavity and subsequently into the other nasal cavity.

In another aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: providing an interface unit, as a

replaceable unit, to an actuation unit, the interface unit including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit, and the actuation unit being configured to actuate the at least one delivery unit of the interface unit; fitting the interface unit to a subject; and actuating the actuation unit to actuate the at least one delivery unit such as to deliver substance to a nasal airway of the subject.

Preferably, the interface unit comprises a disposable unit.

Preferably, the interface unit comprises a single integral unit.

Preferably, the interface unit is packaged in protective packaging, and, prior to the fitting step, the method further comprises the step of: opening the protective packaging.

In one embodiment a plurality of interface units are attached to a belt, and, in the interface unit providing step, a subsequent one of the interface units is provided to the actuation unit.

Preferably, in the interface unit providing step, the actuation unit advances the belt of interface units such as to provide a subsequent one of the interface units thereto.

Preferably, the substance supply unit comprises a substance pump unit for delivering substance, and the substance pump unit includes a chamber containing substance and a piston member which is moved in the chamber to deliver a flow of substance from the chamber.

In one embodiment the substance comprises a liquid.

In another embodiment the substance comprises a powder.

Preferably, the interface unit includes a mouthpiece unit including a mouthpiece, and, prior to the actuation unit actuating step, the method further comprises the step of: the subject exhaling into the mouthpiece.

In one embodiment the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

In one embodiment the at least one delivery unit includes a gas supply unit for supplying a gas flow, and the method further comprises the step of: actuating the gas supply unit to supply a gas flow through the at least one nosepiece unit.

Preferably, the gas supply unit comprises a gas pump unit for delivering a gas flow, and the gas pump unit comprises a cylinder and a piston member which is moved in the cylinder to deliver a gas flow through the at least one nosepiece unit.

In one embodiment, for each delivery unit, the supply of a gas flow is initiated prior to the delivery of substance.

In another embodiment the actuation unit includes a gas supply unit for supplying a gas flow, and the method further comprises the step of: actuating the gas supply unit to supply a gas flow through the at least one nosepiece unit.

In one embodiment, for each delivery unit, the supply of a gas flow is initiated prior to the delivery of substance.

Preferably, the at least one delivery unit is actuated in response to exhalation by the subject.

In one embodiment the actuation unit includes a detection unit for detecting exhalation by the subject and at least one drive unit for actuating the at least one delivery unit; and

the actuation unit actuating step comprises the step of: actuating the at least one drive unit in response to the detection unit detecting exhalation by the subject.

In one embodiment the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the at least one drive unit is actuated in response to detection of a predeterminable pressure by the detection unit.

In another embodiment the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the at least one drive unit is actuated in response to detection of a predeterminable flow rate by the detection unit.

In another embodiment the actuation unit includes at least one drive unit for actuating the at least one delivery unit and a trigger mechanism for actuating the at least one drive unit in response to exhalation by the subject; and the actuation unit actuating step comprises the step of: actuating the trigger mechanism to actuate the at least one drive unit in response to exhalation by the subject.

In one embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

In another embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

Preferably, the interface unit includes first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each including a substance supply unit for delivering substance through the respective nosepiece unit, and the actuation unit actuating step comprises the step of: actuating the actuation unit to actuate the first and second delivery units such as to deliver substance to the respective nasal cavities of the subject.

In one embodiment the first and second delivery units are actuated in succession such that substance is first delivered into one nasal cavity and subsequently into the other nasal cavity.

Preferably, the method is for the mass treatment of subjects, in particular the mass vaccination of subjects.

In a further aspect the present invention provides a nasal delivery component, as a disposable component, comprising at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit.

Preferably, the delivery component is an interface unit for attachment to an actuation unit utilized in actuating the at least one delivery unit.

In one embodiment a plurality of delivery units are attached to a belt such as to allow for successive attachment to the actuation unit.

Preferably, the at least one delivery unit is manually actuatable absent an actuation unit.

Preferably, the delivery component is packaged in protective packaging.

Preferably, the substance supply unit comprises a substance pump unit for delivering substance, the substance pump unit including a chamber containing substance and a piston member which is movable in the chamber to deliver a flow of substance from the chamber.

In one embodiment the substance is a liquid.

In another embodiment the substance is a powder.

Preferably, the delivery component further comprises a mouthpiece unit including a mouthpiece into which the subject in use exhales.

In one embodiment the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

In one embodiment the at least one delivery unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

Preferably, the gas supply unit comprises a gas pump unit for delivering a gas flow, the gas pump unit including a cylinder and a piston member which is movable in the cylinder to deliver a gas flow through the respective nosepiece unit.

In one embodiment the at least one delivery unit is configured such that the gas supply unit initiates supply of a gas flow prior to the substance supply unit delivering substance.

Preferably, the delivery unit comprises first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each for delivering substance through a respective one of the first and second nosepiece units.

Preferably, the delivery component is configured such as to be separable between the first and second nosepiece units, and thereby provide two delivery units which are each separably operable.

In a yet further aspect the present invention provides an actuation unit for receiving and actuating an interface unit, as a replaceable unit, to deliver substance to a nasal airway of a subject, the interface unit including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit, the actuation unit comprising: at least one drive unit for actuating the at least one delivery unit of the interface unit.

Preferably, the interface unit includes a mouthpiece unit including a mouthpiece into which the subject in use exhales.

In one embodiment the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

In one embodiment the actuation unit further comprises: a detection unit for detecting exhalation by the subject into the mouthpiece; and a control unit for actuating the at least one drive unit in response to detecting exhalation by the subject.

In one embodiment the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable pressure by the detection unit.

In another embodiment the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate by the detection unit.

In another embodiment the actuation unit further comprises: a trigger mechanism for actuating the at least one delivery unit in response to exhalation by the subject into the mouthpiece.

In one embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

In another embodiment the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

In one embodiment the at least one delivery unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

In another embodiment the actuation unit further comprises: a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

In one embodiment a plurality of interface units are attached to a belt, and the actuation unit is configured to advance the belt such as successively to provide interface units thereto.

Preferably, the belt to which the interface units are attached is utilized as a guide.

Preferably, the interface unit includes first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each for delivering substance through respective ones of the first and second nosepiece units, and the actuation unit further comprises: first and second drive units for actuating respective ones of the delivery units of the interface unit.

More preferably, the first and second drive units are configured to actuate the substance supply units in succession, and thereby deliver substance first into one nasal cavity and subsequently into the other nasal cavity.

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figure 1 schematically illustrates the anatomy of the upper respiratory tract of a human subject;

Figure 2 illustrates a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 3 illustrates a sectional view through the nosepiece units and delivery units of the interface unit of the delivery device of Figure 2;

Figure 4 illustrates a sectional view through the mouthpiece unit of the interface unit of the delivery device of Figure 2;

Figure 5 schematically represents the actuation unit of the delivery device of Figure 2;

Figures 6(a) to (d) illustrate the operation of the delivery device of Figure 2;

Figures 7(a) and (b) illustrate one modification of the interface unit of the delivery device of Figure 2;

Figure 8 illustrates an interface unit supply as another modification of the delivery device of Figure 2;

Figure 9 illustrates a nasal delivery device in accordance with a second embodiment of the present invention;

Figure 10 illustrates a sectional view through the nosepiece units and delivery units of the interface unit and the actuation unit of the delivery device of Figure 9;

Figure 11 illustrates a sectional view through the mouthpiece unit of the interface unit of the delivery device of Figure 8; and

Figures 12(a) to (e) illustrate the operation of the delivery device of Figure 9.

Figures 2 to 6 illustrate a nasal delivery device in accordance with a first embodiment of the present invention.

The delivery device comprises an interface unit 21 for fitting to a subject and containing the substance to be delivered, and an actuation unit 23 to which the interface unit 21 is

attached to enable the delivery of the substance from the interface unit 21 on exhalation by the subject. In this embodiment the interface unit 21 is a disposable component and the means of attachment of the interface unit 21 to the actuation unit 23 is such as to allow for the easy, repeated attachment of interface units 21 to allow for the treatment of large numbers of subjects, such as in the mass vaccination of subjects.

The interface unit 21 comprises a main body 25 for attachment to the actuation unit 23, in this embodiment as a sliding fit. In an alternative embodiment the main body 25 could be configured to be a clip fit to the actuation unit 23. In this embodiment the means of attachment of the interface unit 21 to the actuation unit 23 is configured, here by the provision of differently-shaped slide features, such as to provide for the attachment of the interface unit 21 to the actuation unit 23 in the correct orient.

The interface unit 21 further comprises first and second nosepiece units 27, 29 for fitting to respective ones of the nostrils of a subject.

The nosepiece units 27, 29 each comprise a cuff member 31, in this embodiment a frusto-conical element, for positioning the respective nosepiece unit 27, 29 in a nasal cavity of the subject and providing a fluid-tight seal therewith, and an outlet unit 33 for delivering substance into the respective nasal cavity of the subject.

Each outlet unit 33 comprises a nozzle 35 from which substance is delivered into the respective nasal cavity of the subject, and a delivery channel 37 through which a gas flow, in this embodiment separate from the exhalation breath of the subject, is delivered to entrain the substance delivered from the nozzle 35.

In this embodiment the nozzle 35 is configured to provide an aerosol spray. In an alternative embodiment, for the delivery of a liquid, the nozzle 35 could be configured to deliver a liquid jet as a column of liquid.

In this embodiment the nozzle 35 is disposed in the delivery channel 37 co-axially with the same. In this embodiment the delivery channel 37 is an annular channel which

surrounds the nozzle 35 such as to define an annular gas flow which entrains the substance delivered from the nozzle 35.

The interface unit 21 further comprises first and second delivery units 39, 41 which are fluidly connected to respective ones of the first and second nosepiece units 27, 29. The delivery units 39, 41 each comprise a substance supply unit 43 for delivering a metered dose of a substance to the respective nozzle 35 and a gas supply unit 45 for delivering a metered volume of a gas, in this embodiment separate to the exhalation breath of the subject, as a gas flow through the respective delivery channel 37. In preferred embodiments the substance comprises a medicament, especially systemic or topical pharmaceuticals, or a vaccine.

In this embodiment each substance supply unit 43 comprises a liquid delivery pump for delivering a metered dose of a substance on actuation thereof, as one of an aerosol spray or a liquid jet as a column of liquid from the respective nozzle 35.

Each substance supply unit 43 comprises a piston unit which comprises a cylinder 47 which defines a chamber 49 and into one, forward end of which a hollow needle 51 extends as an extension of the respective nozzle 35.

Each substance supply unit 43 further comprises first and second pistons 53, 55 which contain a volume of substance therebetween and are movably disposed within the chamber 49.

With this configuration, as illustrated in Figures 6(b) and (c), the forward piston 53 is driven forwardly on the rear piston 55 being driven forwardly, the substance contained between the pistons 53, 55 being substantially incompressible. The forward piston 53 is a puncturable member which is punctured by the needle 51 of the respective nozzle 35 on being driven onto the same, with the needle 51 of the respective nozzle 35 being in fluid communication with the substance contained between the pistons 53, 55 on puncturing the forward piston 53.

In this embodiment the forward piston 53 is spaced from the needle 51 of the respective nozzle 35 by a predetermined distance such that the respective gas supply unit 45 is actuated to commence delivery of a gas flow through the respective delivery channel 37 at least simultaneously with the delivery of substance to the respective nozzle 35, and in a preferred embodiment prior to the delivery of substance to the respective nozzle 35.

In another alternative embodiment each substance supply unit 43 could comprise a powder delivery pump for delivering a metered dose of a dry powder on actuation thereof.

In a further alternative embodiment each substance supply unit 43 could comprise a dry powder delivery unit which delivers a metered dose of a substance, as a dry powder, on actuation thereof.

In another alternative embodiment each substance supply unit 43 could comprise an aerosol canister for delivering a metered volume of a propellant or the like, containing a substance, either as a suspension or solution.

Each gas supply unit 45 comprises a cylinder 57, in this embodiment defined by the main body 25 and being open at the forward end and bounded at the rear end by a rear wall of the main body 25, and a piston 59 which is coupled to the rear piston 55 of the respective substance supply unit 43 and movably disposed within the cylinder 57 between a first, non-actuated position and a second, actuated position such as to drive a volume of gas, in this embodiment about 5 ml, through the respective delivery channel 37 on actuation thereof. Figures 6(b) and 6(c) illustrate the actuation of the gas supply unit 45 of respective ones of the first and second delivery units 39, 41.

The cylinder 57 comprises a first, rear section 57a at which the piston 59 is disposed in the non-actuated position, a second, intermediate section 57b at which the piston 59 is disposed during actuation of the piston 59 and a third, forward section 57c at which the piston 59 is disposed in the actuated position, a port 61 which fluidly connects the rear section 57a to atmosphere, and a clearance hole 63 at the rear end thereof to allow for

the extension of a drive rod 81 of a respective drive unit 75, 77 of the actuation unit 23 therethrough in driving the rear piston 55 of the respective substance supply unit 43 and the piston 59 of the respective gas supply unit 45.

In this embodiment the port 61 is configured to set the flow resistance of a gas flow driven through the respective nosepiece unit 27, 29. In a preferred embodiment the port 61 is fluidly connected to a filter which acts to trap any substance driven through the respective nosepiece unit 27, 29.

In this embodiment the clearance hole 63 is configured to be a sealing fit with a drive rod 81 of a respective drive unit 75, 77 of the actuation unit 23, but need not be a sealing fit, as there is no requirement for a sealing fit. In an alternative embodiment the rear wall of the main body 25, which defines the rear end of each cylinder 57, can comprise a resilient material which is deflected by the drive rod 81 of the respective drive unit 75, 77 of the actuation unit 23.

The rear section 57a of the cylinder 57 has a greater radial dimension than the piston 59 such that, when the piston 59 is in the non-actuated position, an annular channel is defined about the piston 59 in fluid communication with the port 61, whereby a gas flow driven into the respective nosepiece unit 27, 29 from the other nosepiece unit 27, 29 is vented to atmosphere through the port 61. In this embodiment the first and second delivery units 39, 41 are actuated in succession such that the piston 59 of one of the delivery units 39, 41 is in the non-actuated position during actuation of the other of the delivery units 39, 41, thereby providing a flow path through the one nosepiece unit 27, 29.

The intermediate section 57b of the cylinder 57 has the same radial dimension as the piston 59 such that the piston 59 is a sealing fit therein, whereby a gas flow is driven through the respective delivery channel 37 during displacement of the piston 59 thereover. In this embodiment the volume of the gas flow is determined by the length of the intermediate section 57b of the cylinder 57.

The forward section 57c of the cylinder 57 has a greater radial dimension than the piston 59 such that, when the piston 59 is in the actuated position, an annular channel is defined about the piston 59 in fluid communication with the port 61, whereby a gas flow driven into the respective nosepiece unit 27, 29 from the other nosepiece unit 27, 29 is vented to atmosphere through the port 61. In this embodiment, where the first and second delivery units 39, 41 are actuated in succession, the piston 59 of the other of the delivery units 39, 41, that is, the delivery unit 39, 41 which is first actuated, is in the actuated position during actuation of the other of the delivery units 39, 41, thereby providing a flow path to atmosphere through the other nosepiece unit 27, 29.

The piston 59 comprises an annular element 65 and a connecting rod 66 which is coupled to the rear piston 55 of the respective substance supply unit 43. The annular element 65 includes a stepped peripheral edge 67, the peripheral edge 67 including a first, forward section 67a having the same radial dimension as the intermediate section 57b of the cylinder 57 such as to be a sealing fit therewith, and a second, rear section 67b having a smaller radial dimension than the forward section 67a such as to provide an annular flow path about the peripheral edge 67 when the piston 59 is in the actuated position.

In this embodiment the annular element 65 is configured to sealingly engage the rear end of the respective cylinder 57, and thereby close the respective clearance hole 63, when in the non-actuated position.

The interface unit 21 further comprises a mouthpiece unit 69 into which the subject exhales to actuate the actuation unit 23. In this embodiment the mouthpiece unit 69 comprises a mouthpiece 71, here configured to be gripped in the lips of the subject, and a flexible element 73, here a resilient membrane, which is disposed across the rear end of the mouthpiece 71 such as to be acted upon by the exhalation breath of the subject and be deflected thereby. As will be described in more detail hereinbelow, the actuation unit 23 includes a control unit 89 which is actuated by a predetermined deflection of the flexible element 73, which deflection corresponds to the establishment of a

predetermined pressure in the oral cavity of the subject sufficient for closure of the oropharyngeal velum.

The actuation unit 23 comprises a housing 74 to which an interface unit 21 is attachable for the treatment of a subject, the interface unit 21 being a disposable unit, with a fresh interface unit 21 being attached to the housing 74 for each subject to be treated. In this embodiment, in providing that all surfaces, which are brought into contact with a subject or contacted by the exhalation breath of a subject, are confined to the interface unit 21, there is no possibility of cross-contamination of treated subjects.

The actuation unit 23 further comprises first and second drive units 75, 77 for actuating the respective ones of the delivery units 39, 41 of the interface unit 21 in response to exhalation by the subject into the mouthpiece 71.

In this embodiment the drive units 75, 77 each comprise an actuator 79 which includes a drive rod 81, the speed and timing of which is controllable to enable control of the delivery profile of the delivered substance. In a preferred embodiment the actuator 79 comprises a pneumatic actuator.

The actuation unit 23 further comprises a detection unit 83 for detecting the exhalation of the subject into the mouthpiece 71 such as to cause closure of the oropharyngeal velum of the subject. In this embodiment the detection unit 83 comprises a pressure sensor 85 for detecting a pressure developed in the mouthpiece 71, the pressure sensor 85 including a sensing element 87 for sensing the deflection of the resilient element 73 of the mouthpiece unit 69 on exhalation by the subject into the mouthpiece 71. In an alternative embodiment, where the mouthpiece 71 is modified to allow for flow therethrough, the detection unit 83 could comprise a flow sensor for detecting a flow rate developed through the mouthpiece 71 on exhalation by the subject into the mouthpiece 71.

The actuation unit 23 further comprises a control unit 89 which is operably connected to the first and second actuation units 75, 77 and the detection unit 83 such as successively

to actuate the delivery units 39, 41 of the interface unit 21 on exhalation by the subject into the mouthpiece 71 with sufficient force as to maintain the oropharyngeal velum in the closed position. In this embodiment the timing of the actuation of the actuation units 75, 77 and the delivery profile of the actuation units 75, 77 can be controlled by the control unit 89.

In one embodiment the actuation unit 23 can include means for registering each subject being treated, such as by photograph, or fingerprint or iris recognition. By registering the subjects being treated, an accurate treatment record can be maintained.

In a preferred embodiment the actuation unit 23 can include an over-ride facility to enable the actuation of the actuation units 75, 77 irrespective of the development of an exhalation flow by the subject which is sufficient to close the oropharyngeal velum. Although bi-directional delivery through the nasal cavities of a subject is desirable, this over-ride facility can prove useful where subject compliance is poor, such as in infants, and the need for exhalation is not understood.

Operation of the delivery device is illustrated in Figures 6(a) to (d), where Figure 6(a) illustrates the fitting of the nosepiece units 27, 29 to the respective nostrils of a subject, and, following exhalation by the subject into the mouthpiece 71 of the mouthpiece unit 69, Figures 6(b) and (c) illustrate the successive actuation of the first and second delivery units 39, 41, and Figure 6(d) illustrates the state subsequent to delivery.

Figures 7(a) and (b) illustrate an interface unit 21 as one modification of the above-described first embodiment.

In this embodiment the interface unit 21 includes protective packaging 91 which acts to maintain the interface unit 21 sterile prior to use, and can also provide protection for the contained substance, where the substance is sensitive to environmental factors, such as moisture and gas uptake, typically oxygen uptake. Figures 7(a) and (b) illustrate the interface unit 21 with the packaging closed and open respectively.

Figure 8 illustrates an interface unit supply 93 as another modification of the above-described first embodiment.

In this embodiment, instead of the interface units 21 being provided singly, the interface units 21 are mounted on a belt 95 such as to allow for automated or at least semi-automated attachment of the interface units 21 in turn.

In a preferred embodiment the actuation unit 23 can include an advance mechanism which acts to advance each interface unit 21 in turn to the attachment position, with the interface units 21 being guided along a track by the belt 95, whereby the operator is not required to attach the interface units 21, but merely has to perform a supervisory function.

It will be understood that the interface units 21 of the interface unit supply 93 could include protective packaging 91 as in the above-described modification.

Figures 9 to 12 illustrate a nasal delivery device in accordance with a second embodiment of the present invention.

The delivery device comprises an interface unit 121 for fitting to a subject and containing the substance to be delivered, and an actuation unit 123 to which the interface unit 121 is attached to enable the delivery of the substance from the interface unit 121 on exhalation by the subject. In this embodiment the interface unit 121 and the actuation unit 123 are disposable components, and the actuation unit 123, in being of simple construction, enables use in regions which cannot be readily accessed by medical personnel, for example, in remote regions, regions of devastation or regions of epidemic.

The interface unit 121 comprises a main body 125 for attachment to the actuation unit 123, in this embodiment as a sliding fit. In an alternative embodiment the main body 125 could be configured to be a clip fit to the actuation unit 123. In this embodiment the means of attachment of the interface unit 121 to the actuation unit 123 is configured,

here by the provision of differently shaped slide features, such as to provide for the attachment of the interface unit 121 to the actuation unit 123 in the correct orient.

The interface unit 121 further comprises first and second nosepiece units 127, 129 for fitting to respective ones of the nostrils of a subject.

The nosepiece units 127, 129 each comprise a cuff member 131, in this embodiment a frusto-conical element, for positioning the respective nosepiece unit 127, 129 in a nasal cavity of the subject and providing a fluid-tight seal therewith, and an outlet unit 133 for delivering substance into the respective nasal cavity of the subject.

Each outlet unit 133 comprises a nozzle 135 from which substance is delivered into the respective nasal cavity of the subject, and a delivery channel 137 through which a gas flow, in this embodiment separate from the exhalation breath of the subject, is delivered to entrain the substance delivered from the nozzle 135. In an alternative embodiment the interface unit 121 could be configured such that the entraining gas flow is from the exhalation breath of the subject.

In this embodiment the nozzle 135 is configured to provide an aerosol spray. In an alternative embodiment, for the delivery of a liquid, the nozzle 135 could be configured to deliver a liquid jet as a column of liquid.

In this embodiment the nozzle 135 is disposed in the delivery channel 137 co-axially with the same. In this embodiment the delivery channel 137 is an annular channel which surrounds the nozzle 135 such as to define an annular gas flow which entrains the substance delivered from the nozzle 135.

The interface unit 121 further comprises first and second delivery units 139, 141 which are fluidly connected to respective ones of the first and second nosepiece units 127, 129. The delivery units 139, 141 each comprise a substance supply unit 143 for delivering a metered dose of a substance to the respective nozzle 135 and a gas supply unit 145 for delivering a metered volume of a gas, in this embodiment separate to the exhalation

breath of the subject, as a gas flow through the respective delivery channel 137. In preferred embodiments the substance comprises a medicament, especially systemic or topical pharmaceuticals, or a vaccine.

In this embodiment each substance supply unit 143 comprises a liquid delivery pump for delivering a metered dose of a substance on actuation thereof, as one of an aerosol spray or a liquid jet as a column of liquid from the respective nozzle 135.

Each substance supply unit 143 comprises a piston unit which comprises a cylinder 147 which defines a chamber 149 and into one, forward end of which a hollow needle 151 extends as an extension of the respective nozzle 135.

Each substance supply unit 143 further comprises first and second pistons 153, 155 which contain a volume of substance therebetween and are movably disposed within the respective chamber 149.

With this configuration, as illustrated in Figures 12(c) and (d), the forward piston 153 is driven forwardly on the rear piston 155 being driven forwardly, the substance contained between the pistons 153, 155 being substantially incompressible. The forward piston 153 is a puncturable member which is punctured by the needle 151 of the respective nozzle 135 on being driven onto the same, with the needle 151 of the respective nozzle 135 being in fluid communication with the substance contained between the pistons 153, 155 on puncturing the forward piston 153.

In this embodiment the forward piston 153 is spaced from the needle 151 of the respective nozzle 135 by a predetermined distance such that the respective gas supply unit 145 is actuated to commence delivery of a gas flow through the respective delivery channel 137 at least simultaneously with the delivery of substance to the respective nozzle 135, and in a preferred embodiment prior to the delivery of substance to the respective nozzle 135.

In another alternative embodiment each substance supply unit 143 could comprise a powder delivery pump for delivering a metered dose of a dry powder on actuation thereof.

In a further alternative embodiment each substance supply unit 143 could comprise a dry powder delivery unit which delivers a metered dose of a substance, as a dry powder, on actuation thereof.

In another alternative embodiment each substance supply unit 143 could comprise an aerosol canister for delivering a metered volume of a propellant or the like, containing a substance, either as a suspension or solution.

Each gas supply unit 145 comprises a cylinder 157, in this embodiment defined by the main body 125 and being open at the forward end and closed at the rear end by a rear wall of the main body 125, and a piston 159 which is coupled to the rear piston 155 of the respective substance supply unit 143 and movably disposed within the cylinder 157 between a first, non-actuated position and a second, actuated position such as to drive a volume of gas, in this embodiment about 5 ml, through the respective delivery channel 137 on actuation thereof. Figures 12(c) and (d) illustrate the actuation of the gas supply unit 145 of respective ones of the first and second delivery units 139, 141.

The cylinder 157 comprises a first, rear section 157a at which the piston 159 is disposed in the non-actuated position, a second, intermediate section 157b at which the piston 159 is disposed during actuation of the piston 159 and a third, forward section 157c at which the piston 159 is disposed in the actuated position, a port 161 which fluidly connects the rear section 157a to atmosphere, and a clearance hole 163 at the rear end thereof to allow for the extension of a driving rod 181 of a respective drive unit 175, 177 of the actuation unit 123 therethrough in driving the rear piston 155 of the respective substance supply unit 143 and the piston 159 of the respective gas supply unit 145.

In this embodiment the port 161 is configured to set the flow resistance of a gas flow driven through the respective nosepiece unit 127, 129. In a preferred embodiment the

port 161 is fluidly connected to a filter which acts to trap any substance driven through the respective nosepiece unit 127, 129.

In this embodiment the clearance hole 163 is configured to be a sealing fit with a driving rod 181 of a respective drive unit 175, 177 of the actuation unit 123, but in other embodiments need not be a sealing fit, as there is no requirement for a sealing fit. In an alternative embodiment the rear wall of each cylinder 157 can comprise a resilient material which is deflected by the drive rod 181 of the respective drive unit 175, 177 of the actuation unit 123 in driving the rear piston 155 of the respective substance supply unit 143 and the piston 159 of the respective gas supply unit 145.

The rear section 157a of the cylinder 157 has a greater radial dimension than the piston 159 such that, when the piston 159 is in the non-actuated position, an annular channel is defined about the piston 159 in fluid communication with the port 161, whereby a gas flow driven into the respective nosepiece unit 127, 129 from the other nosepiece unit 127, 129 is vented to atmosphere through the port 161. In this embodiment the first and second delivery units 139, 141 are actuated in succession such that the piston 159 of one of the delivery units 139, 141 is in the non-actuated position during actuation of the other of the delivery units 139, 141, thereby providing a flow path through the respective one of the nosepiece units 127, 129.

The intermediate section 157b of the cylinder 157 has the same radial dimension as the piston 159 such that the piston 159 is a sealing fit therein, whereby a gas flow is driven through the respective delivery channel 137 during displacement of the piston 159 thereover. In this embodiment the volume of the gas flow is determined by the length of the intermediate section 157b of the cylinder 157.

The forward section 157c of the cylinder 157 has a greater radial dimension than the piston 159 such that, when the piston 159 is in the actuated position, an annular channel is defined about the piston 159 in fluid communication with the port 161, whereby a gas flow driven into the respective nosepiece unit 127, 129 from the other nosepiece unit 127, 129 is vented to atmosphere through the port 161. In this embodiment, where the

first and second delivery units 139, 141 are actuated in succession, the piston 159 of the other of the delivery units 139, 141, that is, the delivery unit 139, 141 which is first actuated, is in the actuated position during actuation of the other of the delivery units 139, 141, thereby providing a flow path through the other nosepiece unit 127, 129.

The piston 159 comprises an annular element 165 and a connecting rod 166 which is coupled to the rear piston 155 of the respective substance supply unit 143. The annular element 165 includes a stepped peripheral edge 167, the peripheral edge 167 including a first, forward section 167a having the same radial dimension as the intermediate section 157b of the cylinder 157 such as to be a sealing fit therewith, and a second, rear section 167b having a smaller radial dimension than the forward section 167a such as to provide an annular flow path about the peripheral edge 167 when the piston 159 is in the actuated position.

In this embodiment the annular element 165 is configured to sealingly engage the rear end of the respective cylinder 157, and thereby close the respective clearance hole 163, when the piston 159 is in the non-actuated position.

The interface unit 121 further comprises a mouthpiece unit 169 into which the subject exhales to actuate the actuation unit 123. In this embodiment the mouthpiece unit 169 comprises a mouthpiece 171, here configured to be gripped in the lips of the subject, and a flexible element 173, here a resilient membrane, which is disposed across the rear end of the mouthpiece 171 such as to be acted upon by the exhalation breath of the subject and be deflected thereby. As will be described in more detail hereinbelow, the actuation unit 123 includes a trigger mechanism 191 which is actuated by a predetermined deflection of the flexible element 173, which deflection corresponds to the establishment of a predetermined pressure in the oral cavity of the subject sufficient for closure of the oropharyngeal velum. Figure 12(b) illustrates the state where a subject is exhaling into the mouthpiece 171 of the mouthpiece unit 169 such as to cause deflection of the flexible element 173, but prior to the actuation of the delivery units 139, 141.

The actuation unit 123 comprises a housing 174 to which an interface unit 121 is attachable for the treatment of a subject.

The actuation unit 123 further comprises first and second drive units 175, 177 which are actuatable to actuate respective ones of the delivery units 139, 141 in response to exhalation by the subject. Figures 12(b) and (e) illustrate the first and second drive units 175, 177 in respective ones of the loaded, but non-actuated and actuated configurations.

The drive units 175, 177 each comprise a drive member 179 which is movable between a rest position in which the respective delivery unit 139, 141 is in the non-actuated position and a second, actuated position in which the piston 159 of the respective gas piston 145 and the rear piston 155 of the respective substance supply unit 143 are advanced to the actuated position. In this embodiment the drive member 179 includes a drive rod 181 which extends through the respective clearance aperture 163 in the main body 125.

The drive units 175, 177 each further comprise a load biasing element 183, in this embodiment a resilient element, particularly a compression spring, for biasing the respective drive member 179 in an actuating direction when in the rest position.

The actuation unit 123 further comprises a loading assembly 185 for commonly loading the load biasing element 183 of each of the drive units 175, 177 such as to bias the drive member 179 of each of the drive units 175, 177 when in the rest position with an actuation force.

The loading assembly 185 comprises a loading block 187 which is commonly coupled to the load biasing elements 183 of the drive units 175, 177, and a loading member 189, in this embodiment a lever, for moving the loading block 187 between a first, inoperative position in which the load biasing elements 183 are not loaded thereby, and a second, operative position in which the load biasing elements 183, when restrained, load the respective drive members 179 with the actuation force.

The actuation unit 123 further comprises a trigger mechanism 191 which is configured normally to lock the drive members 179 of the drive units 175, 177 in the rest position and release the same in succession on exhalation by the subject through the mouthpiece 171, which drive members 179, as loaded by the respective load biasing elements 183, once released act commonly to actuate the respective delivery units 139, 141.

In this embodiment the trigger mechanism 191 is configured to cause successive actuation of the drive units 175, 177 on generation of a predetermined pressure within the mouthpiece 171. Figures 12(c) and 12(d) illustrate the actuation of respective ones of the first and second drive units 175, 177.

In another embodiment the trigger mechanism 191 could be configured to cause the successive actuation of the drive units 175, 177 on generation of a predetermined flow rate through the mouthpiece 171.

The trigger mechanism 191 comprises a release element 193, here a slideable element including a lateral projection 195, which is disposed such as to be engaged by the flexible element 173 of the mouthpiece unit 169 on deflection of the same by the subject exhaling into the mouthpiece 171 at a predetermined pressure and moved from a first, locking position, as illustrated in Figure 12(a), in which the release element 193 acts to lock the trigger mechanism 191 to prevent actuation of the same and a second, release position, as illustrated in Figure 12(b), in which the trigger mechanism 191 is released to enable successive actuation of the delivery units 139, 141.

In this embodiment the trigger mechanism 191 further comprises a biasing element 194, in this embodiment a resilient element, particularly a compression spring, for biasing the release element 193 to the locking position, so as to apply a predetermined actuation force to the flexible element 173 in the mouthpiece 171 of the mouthpiece unit 169 and thereby require a predetermined actuation pressure to be developed in the mouthpiece 171 prior to actuation of the trigger mechanism 191.

The trigger mechanism 191 further comprises a linkage assembly 197 which includes first and second link elements 199, 201, which, when in a locking configuration, act to support the drive member 179 of the first drive unit 175 in the rest position and prevent movement thereof when loaded by the respective load biasing element 183. The linkage assembly 197 is maintained in the locking configuration by the lateral projection 195 of the release element 193 when in the locking position. One of the link elements 199 is pivotally coupled at one end to the drive member 179 of the first drive unit 175, and the other of the link elements 201 is pivotally coupled at one end to the other end of the first link element 199 and at the other end to the housing 174.

The trigger mechanism 191 further comprises a biasing element 203, in this embodiment a resilient element, particularly a compression spring, for biasing the linkage assembly 197 from the locking configuration, such that, on movement of the release element 193 from the locking position to the release position through deflection of the flexible element 173 in the mouthpiece 171 of the mouthpiece unit 169, as illustrated in Figures 12(a) and (b), the biasing element 203 acts to collapse the linkage assembly 197, with which collapse the drive member 179 of the first drive unit 175 is driven by the load biasing element 183 thereof to actuate the first delivery unit 139, as illustrated in Figure 12(c).

The trigger mechanism 191 further comprises a lever assembly 205, which, when in a locking position, as illustrated in Figure 12(b), acts to support the drive member 179 of the second drive unit 177 in the rest position and prevent movement thereof when loaded by the respective load biasing element 183.

In this embodiment the lever assembly 205 comprises an L-shaped lever 206 which includes first and second arms 207, 209.

One arm 207 of the lever 206 is mounted at one end thereof about a pivot 211 such as to be rotatable between a locking position, as illustrated in Figure 12(b), in which the distal end of the one arm 207 engages the drive member 179 of the second drive unit 177 such as to prevent movement thereof when loaded by the respective load biasing element 183,

and a release position, as illustrated in Figure 12(c), in which the lever 206 is rotated such as to release the drive member 179 of the second drive unit 177 from the locking position and thereby actuate the second delivery unit 141, as illustrated in Figure 12(d).

In this embodiment the lever assembly 205 includes a stop 213 which acts as an abutment against which the lever 206 is supported in the locking position, and a biasing element 215, here a compression spring, for biasing the lever 206 to the locking position.

The other arm 209 of the lever 206 is configured to be engaged by the linkage assembly 197 when the drive member 183 of the first drive unit 175 approaches the actuated position, as illustrated in Figure 12(c), which engagement acts to rotate the lever 206 to move the lever 206 to the release position, in which position the load biasing element 183 of the second drive unit 177 acts to drive the drive member 179 thereof to the actuated position and thereby actuate the second delivery unit 141.

Operation of the delivery device is illustrated in Figures 12(a) to (e), where Figure 12(a) illustrates the priming of the delivery device and the fitting of the nosepiece units 127, 129 to the respective nostrils of a subject, and, following exhalation by the subject into the mouthpiece 171 of the mouthpiece unit 169, Figure 12(b) illustrates the state where a sufficient pressure has been developed in the mouthpiece 171 as to cause deflection of the flexible element 173 in the mouthpiece 171 and allow actuation of the trigger mechanism 191, Figures 12(c) and (d) illustrate the successive actuation of the first and second delivery units 139, 141, and Figure 12(e) illustrates the state subsequent to delivery.

Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined by the appended claims.

For example, the delivery device of the first described embodiment could be modified such that the entraining gas flow is supplied by the actuation unit 23. In this modification, the interface unit 21 is modified to omit the gas supply units 45, with the

pistons 59 of the interface unit 21 in this embodiment being modified to omit the annular elements 65 thereof, and the actuation unit 23 is modified to include a gas supply unit for selectively supplying a gas flow to the delivery channels 37 of the nosepiece units 27, 29 through the ports 61, the gas supply unit being configured to vent to atmosphere the other of the ports 61 than to which the gas flow is being supplied. This configuration enables a high flow rate to be developed, where desired. In a preferred embodiment the gas supply unit includes a one-way check valve to prevent back-flow thereinto of gas which has been exposed to the nasal airway of a subject.

In another modification, the interface units 21, 121 of the described embodiments can be configured such as to allow the interface units 21, 121 to be broken along a line between the nosepiece units 27, 29, 127, 129, and thereby allow for the separation of the delivery units 39, 41, 139, 141. In this way, the delivery units 39, 41, 139, 141 can be used to deliver single doses of substance to subjects where an actuation unit 23, 123 is not available.

In a further modification, the interface units 21, 121 can be modified to omit the rear wall of the main body 25, 125 adjacent the gas supply units 45, 145 such as to allow for the manual actuation of the delivery units 39, 41, 139, 141 by depression of the respective piston 59, 159. Such manual actuation of the delivery units 39, 41, 139, 141 would also be possible where the rear wall of the main body 25, 125 adjacent the gas supply units 45, 145 is a flexible element, typically a resilient element, or where the pistons 59, 159 include an actuation rod which extends through the respective clearance aperture 63, 163, with manual actuation of the delivery units 39, 41, 139, 141 being achieved by depression of the respective actuation rod. This modification would also extend to delivery units 39, 41, 139, 141 which include no piston 59, 159.

In a yet further modification, the interface units 21, 121 can include only one nosepiece unit 27, 29, 127, 129 and associated delivery unit 39, 41, 139, 141. In one embodiment the mouthpiece 71, 171 can be fluidly connected to the delivery channel 37, 137 of the one nosepiece unit 27, 29, 127, 129, with the exhalation breath of a subject providing the entraining gas flow. Such an embodiment provides for both automated actuation by an

actuation unit 23, 123 where deflection of the flexible element 73, 173 of the mouthpiece unit 69, 169 acts to actuate the actuation unit 23, 123, and manual actuation where the subject simultaneously exhales and manual actuates a delivery unit 39, 41, 139, 141.

In the described embodiments the mouthpieces 71, 171 are configured to be gripped in the lips of a subject. In alternative embodiments the mouthpieces 71, 171 could be configured to be gripped by the teeth of a subject and sealed by the lips of the subject. In preferred embodiments the mouthpieces 71, 171 could be specifically configured to have one or both of a shape or geometry which allows the delivery devices to be gripped repeatedly in the same position, thereby providing for the respective nosepiece units 27, 29, 127, 129 to be reliably inserted in the same position in the nasal cavity.

In preferred embodiments the delivery units are configured to deliver substance through one nostril of a subject at such a pressure as to flow around the posterior margin of the nasal septum and out of the other nostril of the subject, thereby achieving bi-directional delivery through the nasal cavities as disclosed in WO-A-00/51672. In alternative embodiments the delivery units could be configured to deliver substance at a reduced pressure which is not sufficient to achieve bi-directional delivery through the nasal cavities. Such embodiments are still advantageous as compared to known delivery devices in providing for velum closure.

CLAIMS

1. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
an interface unit, as a replaceable unit, including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit; and
an actuation unit for actuating the at least one delivery unit of the interface unit.

2. The delivery device of claim 1, wherein the interface unit comprises a disposable unit.

3. The delivery device of claim 1 or 2, wherein the interface unit comprises a single integral unit.

4. The delivery device of any of claims 1 to 3, wherein the interface unit is packaged in protective packaging.

5. The delivery device of any of claims 1 to 4, comprising:
a plurality of interface units attached to a belt such as to allow for successive attachment of the interface units to the actuation unit.

6. The delivery device of claim 5, wherein the actuation unit is configured successively to provide the interface units thereto through use of the belt as a guide.

7. The delivery device of any of claims 1 to 6, wherein the substance supply unit comprises a substance pump unit for delivering substance, the substance pump unit including a chamber containing substance and a piston member which is movable in the chamber to deliver a flow of substance from the chamber.

8. The delivery device of claim 7, wherein the substance comprises a liquid.

9. The delivery device of claim 7, wherein the substance comprises a powder.

10. The delivery device of any of claims 1 to 9, wherein the interface unit includes a mouthpiece unit including a mouthpiece into which the subject in use exhales.

11. The delivery device of claim 10, wherein the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by a subject into the mouthpiece.

12. The delivery device of any of claims 1 to 11, wherein the at least one delivery unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

13. The delivery device of claim 12, wherein the gas supply unit comprises a gas pump unit for delivering a gas flow, the gas pump unit comprising a cylinder and a piston member which is movable in the cylinder to deliver a gas flow through the at least one nosepiece unit.

14. The delivery device of claim 12 or 13, wherein the at least one delivery unit is configured such that the gas supply unit initiates supply of a gas flow prior to actuation of the substance supply unit to deliver substance.

15. The delivery device of any of claims 1 to 11, wherein the actuation unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

16. The delivery device of claim 15, wherein the actuation unit is configured such that the gas supply unit initiates supply of a gas flow prior to actuation of the substance supply unit to deliver substance.

17. The delivery device of any of claims 1 to 16, wherein the at least one delivery unit is actuated in response to exhalation by the subject.

18. The delivery device of claim 17, wherein the actuation unit includes a detection unit for detecting exhalation by the subject, at least one drive unit for actuating the at least one delivery unit, and a control unit for actuating the at least one drive unit in response to detecting exhalation by the subject.

19. The delivery device of claim 18, wherein the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable pressure by the detection unit.

20. The delivery device of claim 18, wherein the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate by the detection unit.

21. The delivery device of claim 17, wherein the actuation unit includes at least one drive unit for actuating the at least one delivery unit, and a trigger mechanism for actuating the at least one drive unit in response to exhalation by the subject into the mouthpiece.

22. The delivery device of claim 21, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

23. The delivery device of claim 21, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

24. The delivery device of any of claims 1 to 23, wherein the interface unit includes first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each including a substance supply unit for delivering substance through the respective nosepiece unit.

25. The delivery device of claim 24, wherein the actuation unit is configured to actuate the first and second delivery units in succession such that substance is first delivered into one nasal cavity and subsequently into the other nasal cavity.

26. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
providing an interface unit, as a replaceable unit, to an actuation unit, the interface unit including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit, and the actuation unit being configured to actuate the at least one delivery unit of the interface unit;
fitting the interface unit to a subject; and
actuating the actuation unit to actuate the at least one delivery unit such as to deliver substance to a nasal airway of the subject.

27. The method of claim 26, wherein the interface unit comprises a disposable unit.

28. The method of claim 26 or 27, wherein the interface unit comprises a single integral unit.

29. The method of any of claims 26 to 28, wherein the interface unit is packaged in protective packaging, and, prior to the fitting step, further comprising the step of: opening the protective packaging.

30. The method of any of claims 26 to 29, wherein a plurality of interface units are attached to a belt, and, in the interface unit providing step, a subsequent one of the interface units is provided to the actuation unit.

31. The method of claim 30, wherein, in the interface unit providing step, the actuation unit advances the belt of interface units such as to provide a subsequent one of the interface units thereto.

32. The method of any of claims 26 to 31, wherein the substance supply unit comprises a substance pump unit for delivering substance, and the substance pump unit includes a chamber containing substance and a piston member which is moved in the chamber to deliver a flow of substance from the chamber.

33. The method of claim 32, wherein the substance comprises a liquid.

34. The method of claim 32, wherein the substance comprises a powder.

35. The method of any of claims 26 to 34, wherein the interface unit includes a mouthpiece unit including a mouthpiece, and, prior to the actuating unit actuating step, further comprising the step of:
the subject exhaling into the mouthpiece.

36. The method of claim 35, wherein the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

37. The method of any of claims 26 to 36, wherein the at least one delivery unit includes a gas supply unit for supplying a gas flow, and further comprising the step of:
actuating the gas supply unit to supply a gas flow through the at least one nosepiece unit.

38. The method of claim 37, wherein the gas supply unit comprises a gas pump unit for delivering a gas flow, and the gas pump unit comprises a cylinder and a piston member which is moved in the cylinder to deliver a gas flow through the at least one nosepiece unit.

39. The method of claim 37 or 38, wherein, for each delivery unit, the supply of a gas flow is initiated prior to the delivery of substance.

40. The method of any of claims 26 to 36, wherein the actuation unit includes a gas supply unit for supplying a gas flow, and further comprising the step of:
actuating the gas supply unit to supply a gas flow through the at least one nosepiece unit.

41. The method of claim 40, wherein, for each delivery unit, the supply of a gas flow is initiated prior to the delivery of substance.

42. The method of any of claims 26 to 41, wherein the at least one delivery unit is actuated in response to exhalation by the subject.

43. The method of claim 42, wherein the actuation unit includes a detection unit for detecting exhalation by the subject and at least one drive unit for actuating the at least one delivery unit; and the actuation unit actuating step comprises the step of:
actuating the at least one drive unit in response to the detection unit detecting exhalation by the subject.

44. The method of claim 43, wherein the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the at least one drive unit is actuated in response to detection of a predeterminable pressure by the detection unit.

45. The method of claim 43, wherein the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the at least one drive unit is

actuated in response to detection of a predeterminable flow rate by the detection unit.

46. The method of claim 42, wherein the actuation unit includes at least one drive unit for actuating the at least one delivery unit and a trigger mechanism for actuating the at least one drive unit in response to exhalation by the subject; and the actuation unit actuating step comprises the step of:
actuating the trigger mechanism to actuate the at least one drive unit in response to exhalation by the subject.

47. The method of claim 46, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

48. The method of claim 46, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

49. The method of any of claims 26 to 48, wherein the interface unit includes first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each including a substance supply unit for delivering substance through the respective nosepiece unit, and the actuation unit actuating step comprises the step of:
actuating the actuation unit to actuate the first and second delivery units such as to deliver substance to the respective nasal cavities of the subject.

50. The method of claim 49, wherein the first and second delivery units are actuated in succession such that substance is first delivered into one nasal cavity and subsequently into the other nasal cavity.

51. The method of any of claims 26 to 50, where the method is for the mass treatment of subjects, in particular the mass vaccination of subjects.

52. A nasal delivery component, as a disposable component, comprising at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit.

53. The delivery component of claim 52, wherein the delivery component is an interface unit for attachment to an actuation unit utilized in actuating the at least one delivery unit.

54. The delivery component of claim 53, wherein a plurality of delivery units are attached to a belt such as to allow for successive attachment to the actuation unit.

55. The delivery component of claim 53 or 54, wherein the at least one delivery unit is manually actuatable absent an actuation unit.

56. The delivery component of any of claims 52 to 55, wherein the delivery component is packaged in protective packaging.

57. The delivery component of any of claims 52 to 56, wherein the substance supply unit comprises a substance pump unit for delivering substance, the substance pump unit including a chamber containing substance and a piston member which is movable in the chamber to deliver a flow of substance from the chamber.

58. The delivery component of claim 57, wherein the substance is a liquid.

59. The delivery component of claim 57, wherein the substance is a powder.

60. The delivery component of any of claims 52 to 59, further comprising a mouthpiece unit including a mouthpiece into which the subject in use exhales.

61. The delivery component of claim 60, wherein the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

62. The delivery component of any of claims 52 to 61, wherein the at least one delivery unit includes a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

63. The delivery component of claim 62, wherein the gas supply unit comprises a gas pump unit for delivering a gas flow, the gas pump unit including a cylinder and a piston member which is movable in the cylinder to deliver a gas flow through the respective nosepiece unit.

64. The delivery component of claim 63, wherein the at least one delivery unit is configured such that the gas supply unit initiates supply of a gas flow prior to the substance supply unit delivering substance.

65. The delivery component of any of claims 52 to 64, comprising first and second nosepiece units for fitting to respective nostrils of the subject, and first and second delivery units, each for delivering substance through a respective one of the first and second nosepiece units.

66. The delivery component of claim 65, where configured such as to be separable between the first and second nosepiece units, and thereby provide two delivery units which are each separably operable.

67. An actuation unit for receiving and actuating an interface unit, as a replaceable unit, to deliver substance to a nasal airway of a subject, the interface unit including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit, the actuation unit comprising:

at least one drive unit for actuating the at least one delivery unit of the interface unit.

68. The actuation unit of claim 67, wherein the interface unit includes a mouthpiece unit including a mouthpiece into which the subject in use exhales.

69. The actuation unit of claim 68, wherein the mouthpiece is fluidly connected to the at least one nosepiece unit such as to provide an air flow therethrough on exhalation by the subject into the mouthpiece.

70. The actuation unit of claim 68 or 69, further comprising:
a detection unit for detecting exhalation by a subject into the mouthpiece; and
a control unit for actuating the at least one drive unit in response to detecting exhalation by the subject.

71. The actuation unit of claim 70, wherein the detection unit includes a pressure sensor for detecting a pressure in the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable pressure by the detection unit.

72. The actuation unit of claim 70, wherein the detection unit includes a flow sensor for detecting a flow rate through the mouthpiece, and the control unit is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate by the detection unit.

73. The actuation unit of claim 68 or 69, further comprising:
a trigger mechanism for actuating the at least one delivery unit in response to exhalation by the subject into the mouthpiece.

74. The actuation unit of claim 73, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to generation of a predeterminable pressure in the mouthpiece.

75. The actuation unit of claim 73, wherein the trigger mechanism is configured to actuate the at least one drive unit in response to detection of a predeterminable flow rate through the mouthpiece.

76. The actuation unit of any of claims 67 to 75, wherein the at least one delivery unit includes a gas supply unit for supplying a gas flow through a respective nosepiece unit.

77. The actuation unit of any of claims 67 to 75, further comprising:
a gas supply unit for supplying a gas flow through the at least one nosepiece unit.

78. The actuation unit of any of claims 67 to 77, wherein a plurality of interface units are attached to a belt, and the actuation unit is configured to advance the belt such as successively to provide interface units thereto.

79. The actuation unit of claim 78, wherein the belt to which the interface units are attached is utilized as a guide.

80. The actuation unit of any of claims 67 to 79, wherein the interface unit includes first and second nosepiece units for fitting to respective nostrils of a subject, and first and second delivery units, each for delivering substance through respective ones of the first and second nosepiece units, and further comprising:
first and second drive units for actuating respective ones of the delivery units of the interface unit.

81. The actuation unit of claim 80, wherein the first and second drive units are configured to actuate the substance supply units in succession, and thereby deliver substance first into one nasal cavity and subsequently into the other nasal cavity.

82. A nasal delivery device for delivering substance to a nasal airway of a subject substantially as hereinbefore described with reference to Figures 2 to 5 or Figures 8 to 12, optionally in conjunction with Figures 6 and 7, of the accompanying drawings.

83. A method of delivering substance to a nasal airway of a subject substantially as hereinbefore described with reference to Figures 2 to 5 or Figures 8 to 12, optionally in conjunction with Figures 6 and 7, of the accompanying drawings.

84. A nasal delivery component substantially as hereinbefore described with reference to Figures 2 to 5 or Figures 8 to 12, optionally in conjunction with Figures 6 and 7, of the accompanying drawings.

85. An actuation unit for receiving and actuating an interface unit to deliver substance to a nasal airway of a subject substantially as hereinbefore described with reference to Figures 2 to 5 or Figures 8 to 12, optionally in conjunction with Figures 6 and 7, of the accompanying drawings.

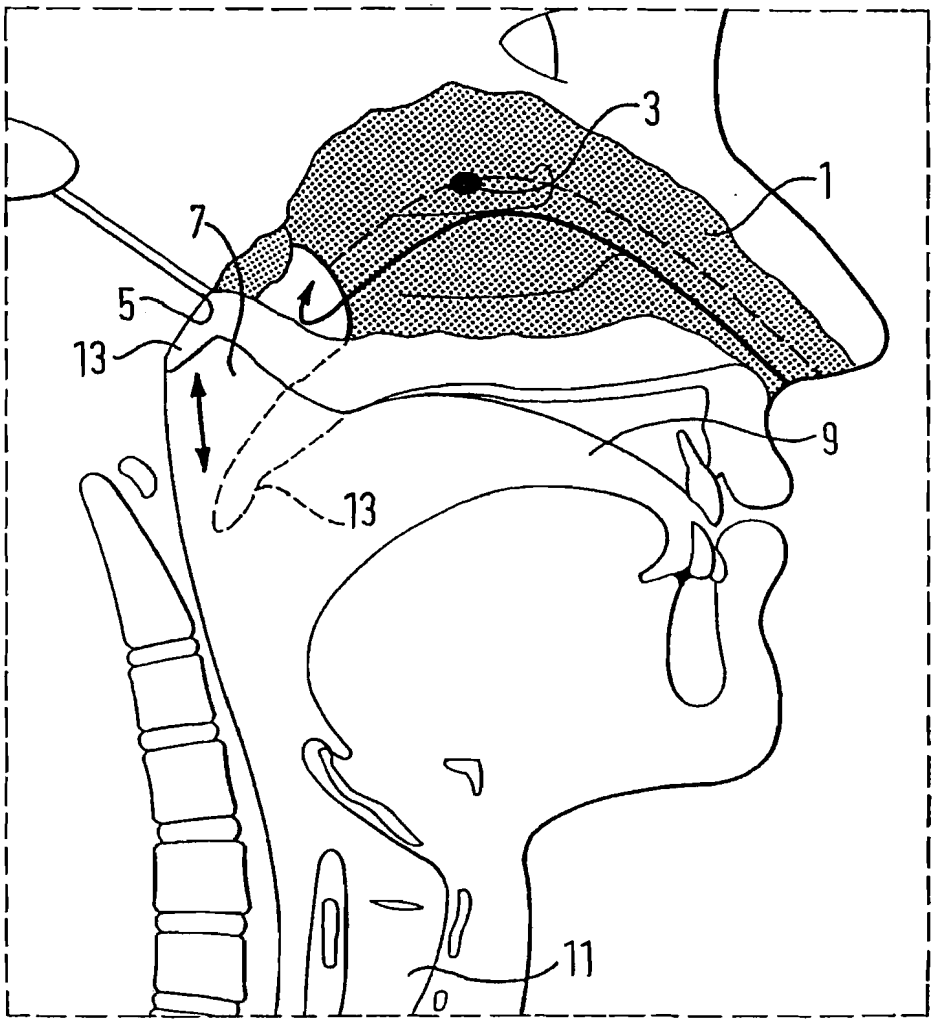


FIG. 1

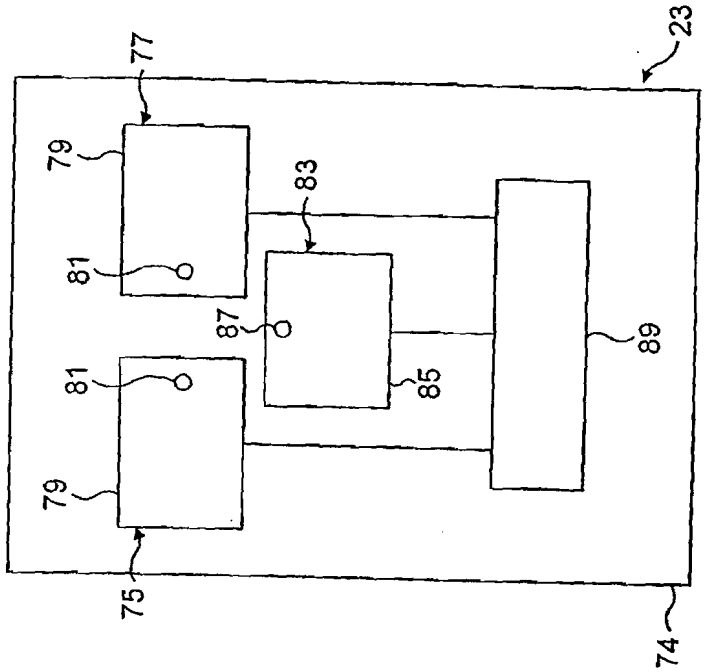


FIG. 5

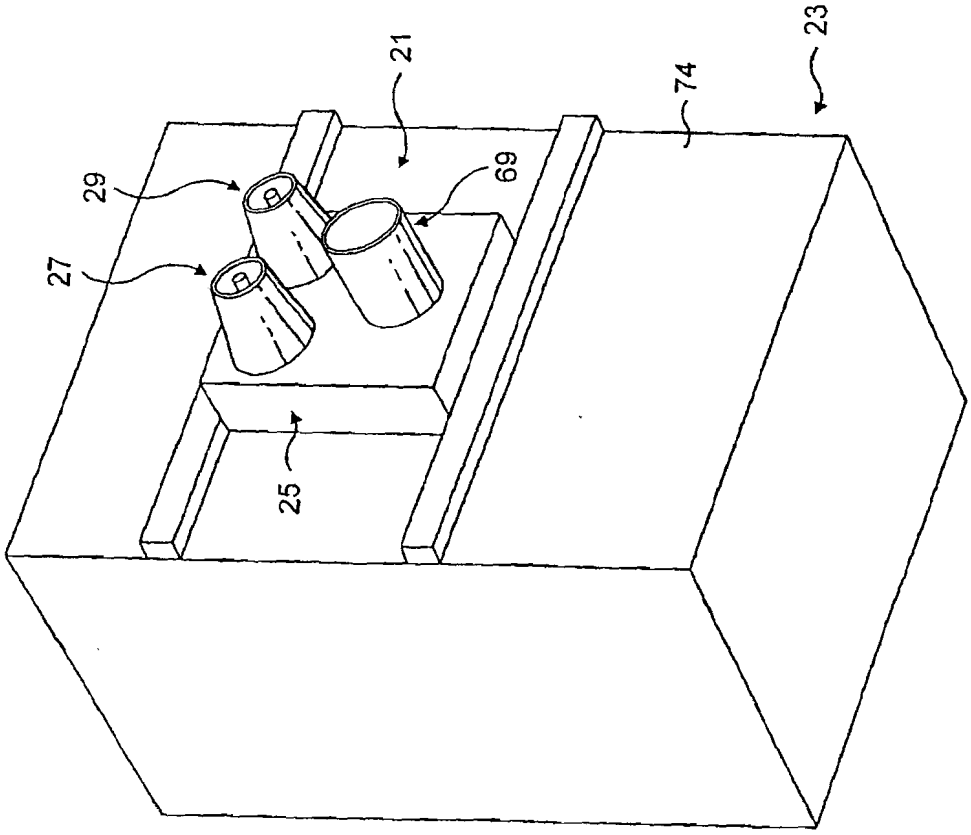


FIG. 2

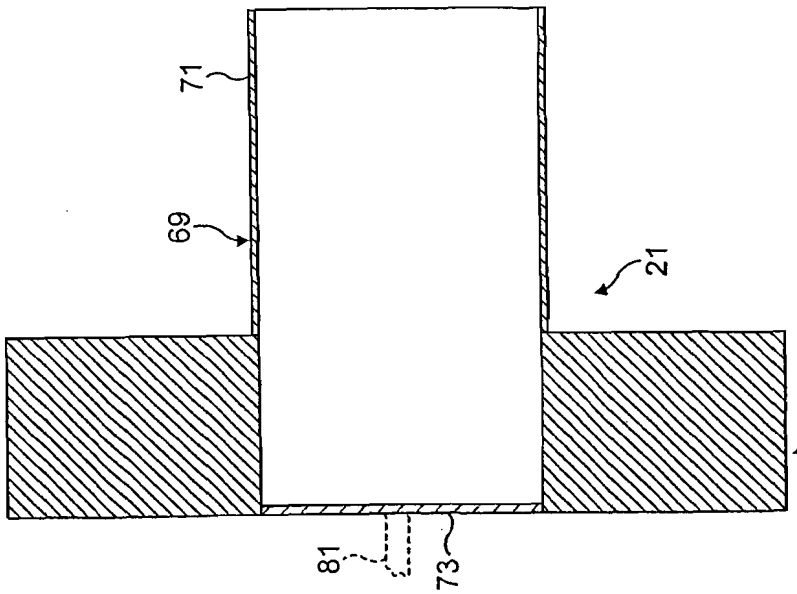

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FIG. 4

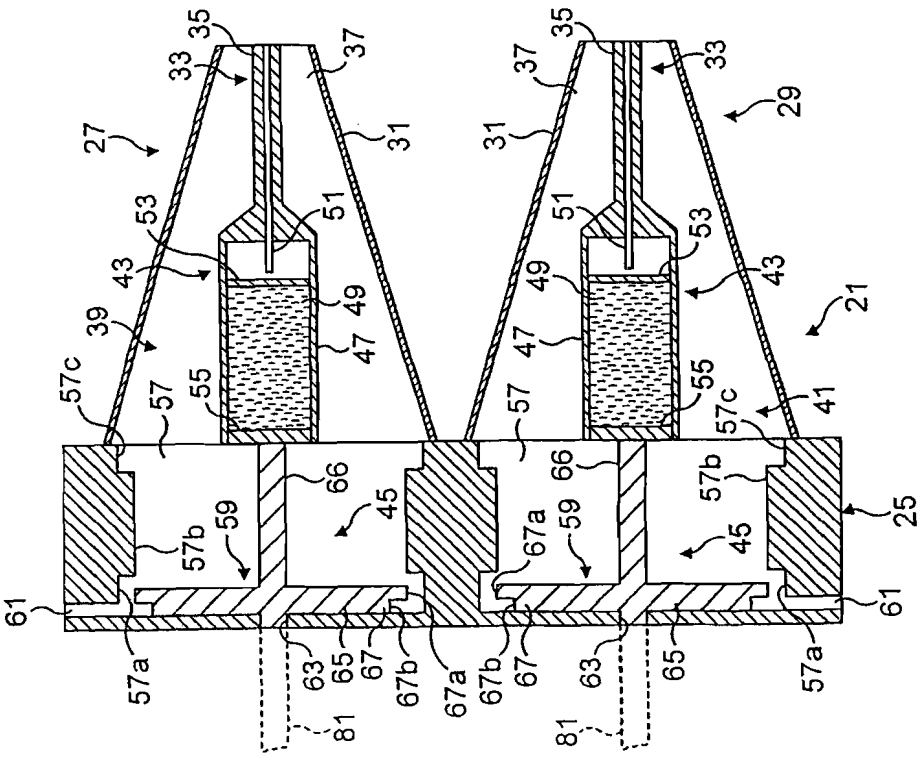
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FIG. 3

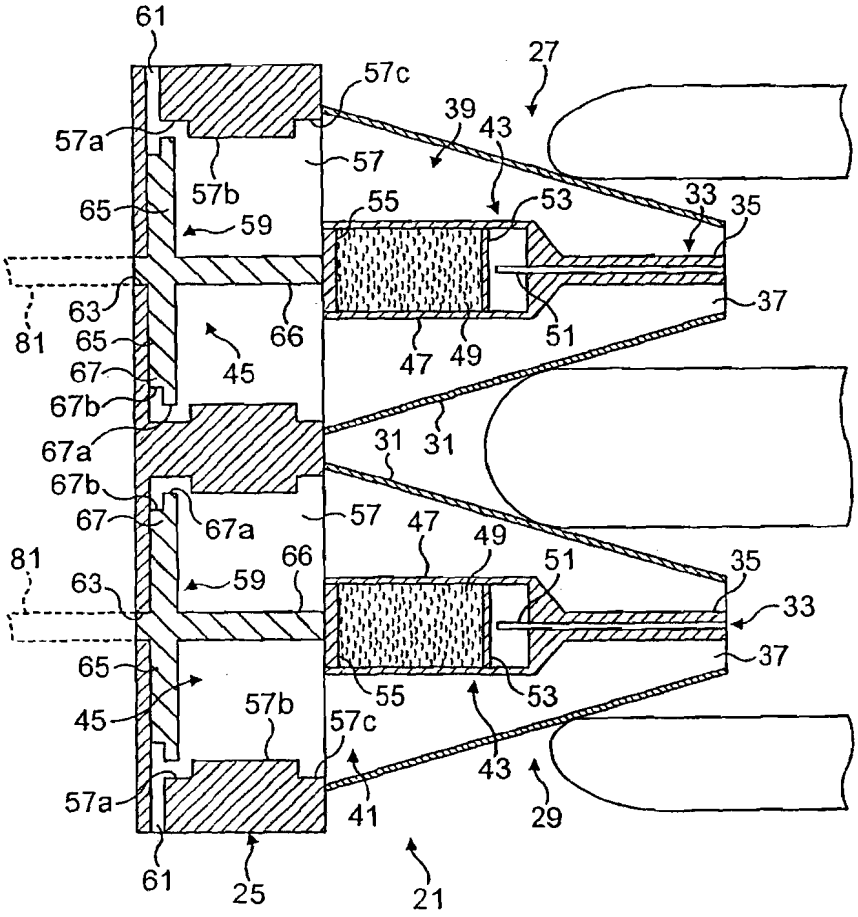
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FIG. 6(a)

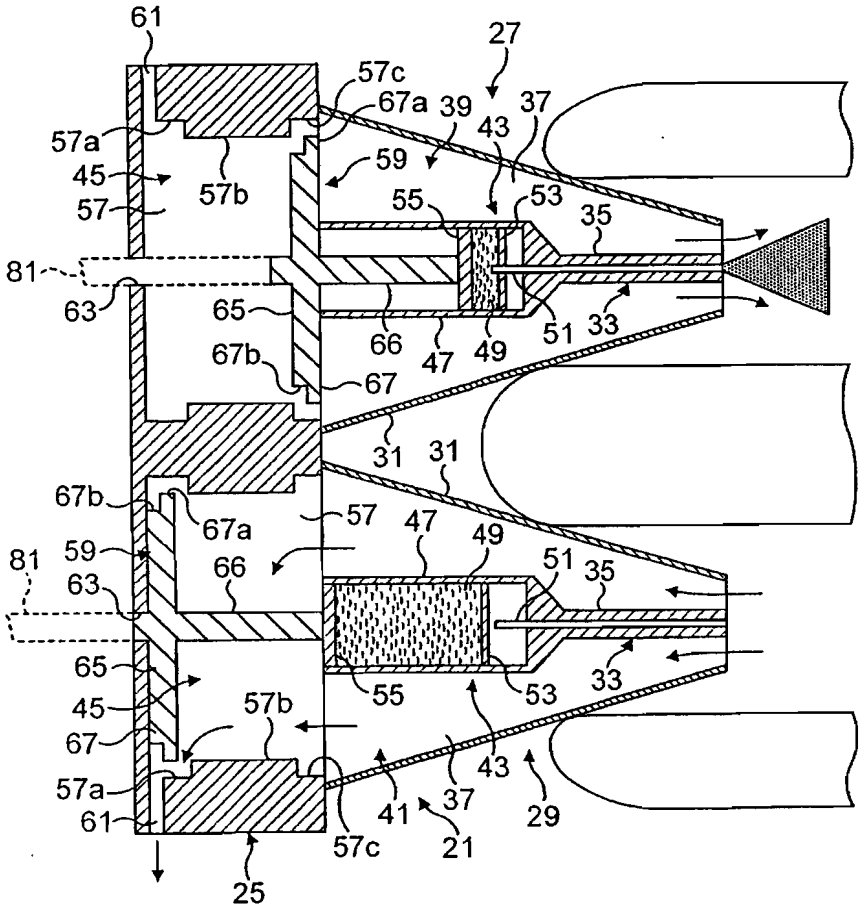
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FIG. 6(b)

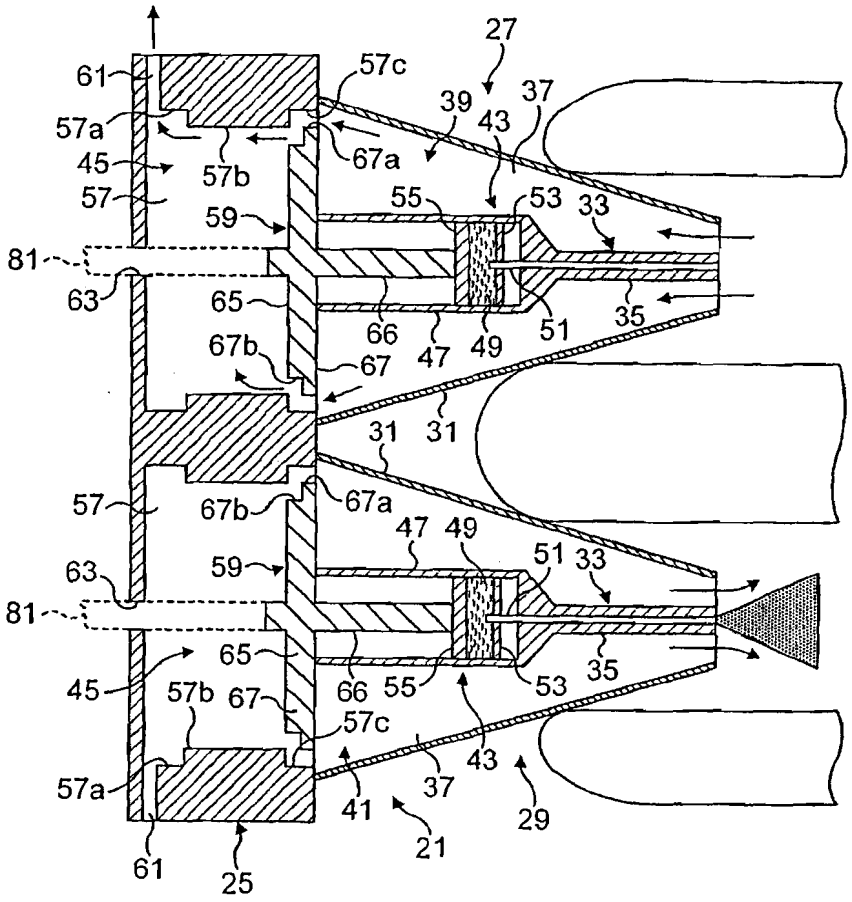
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FIG. 6(c)

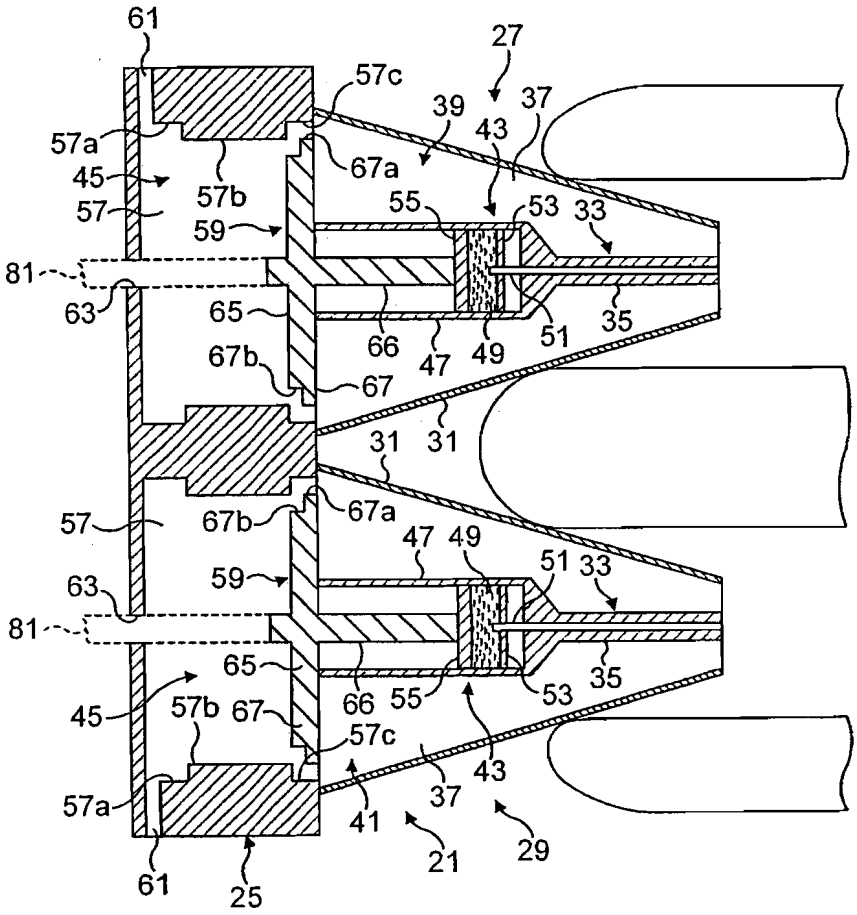
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FIG. 6(d)

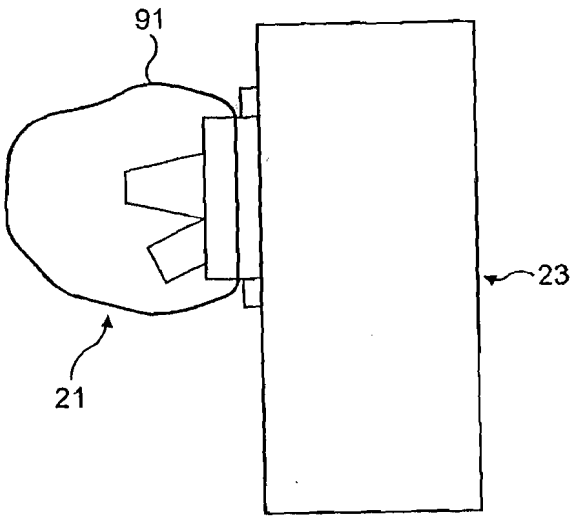

FIG. 7(a)

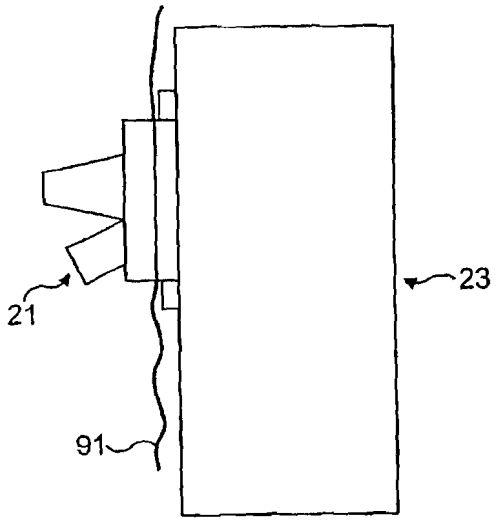

FIG. 7(b)

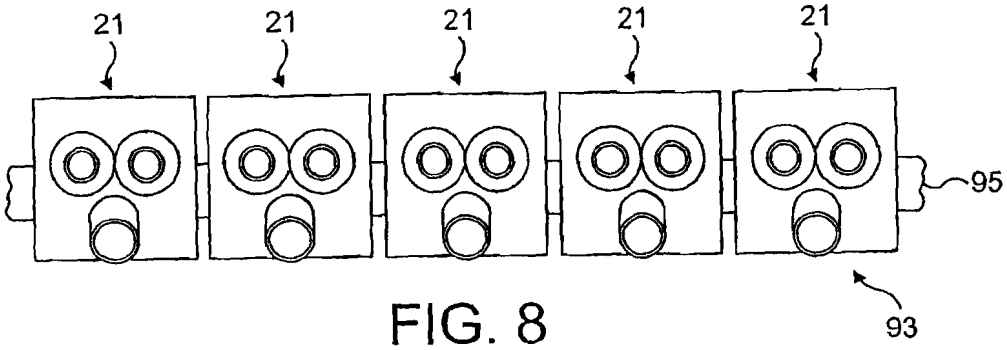

FIG. 8

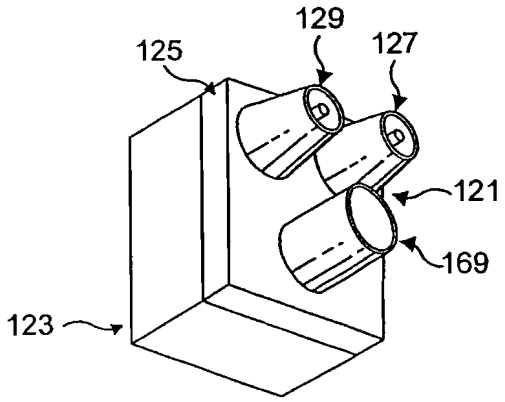

FIG. 9

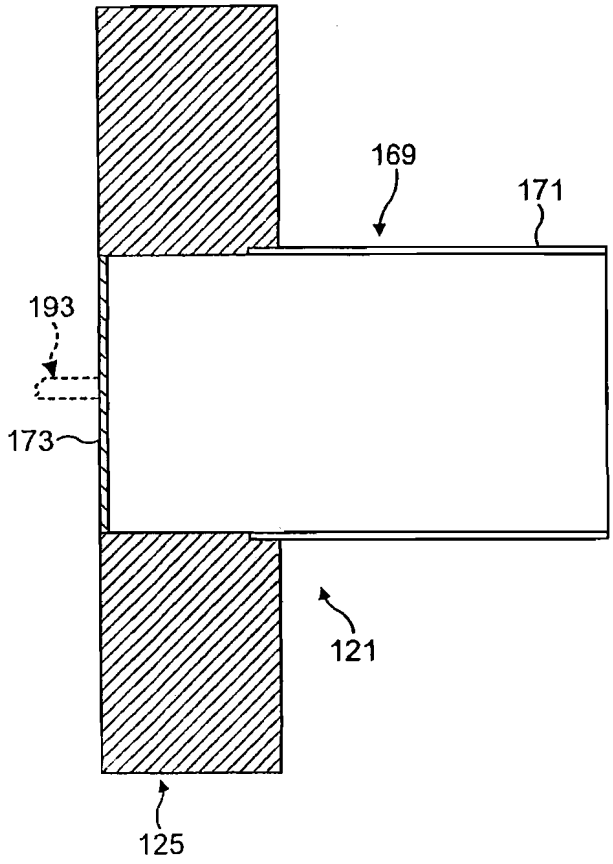

FIG. 11

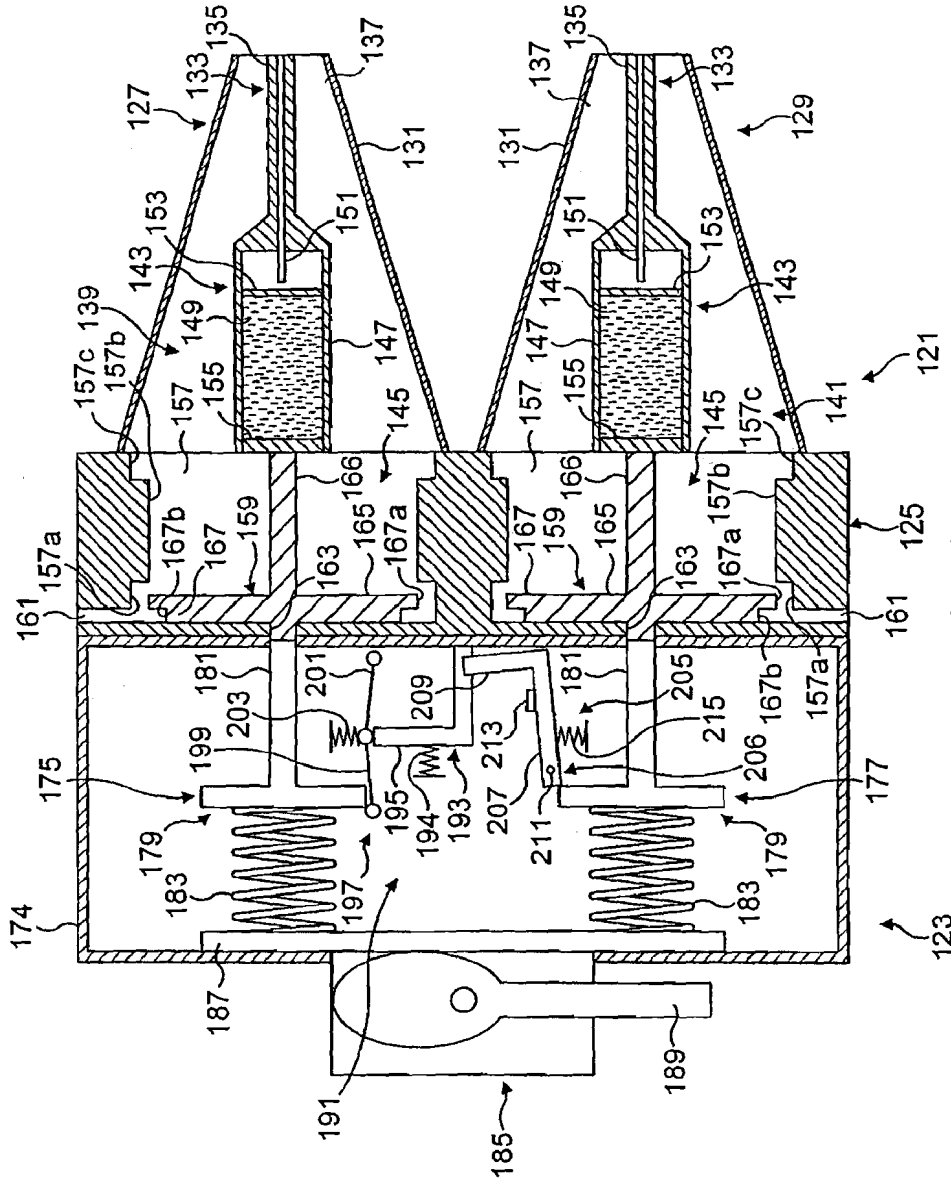
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FIG. 10

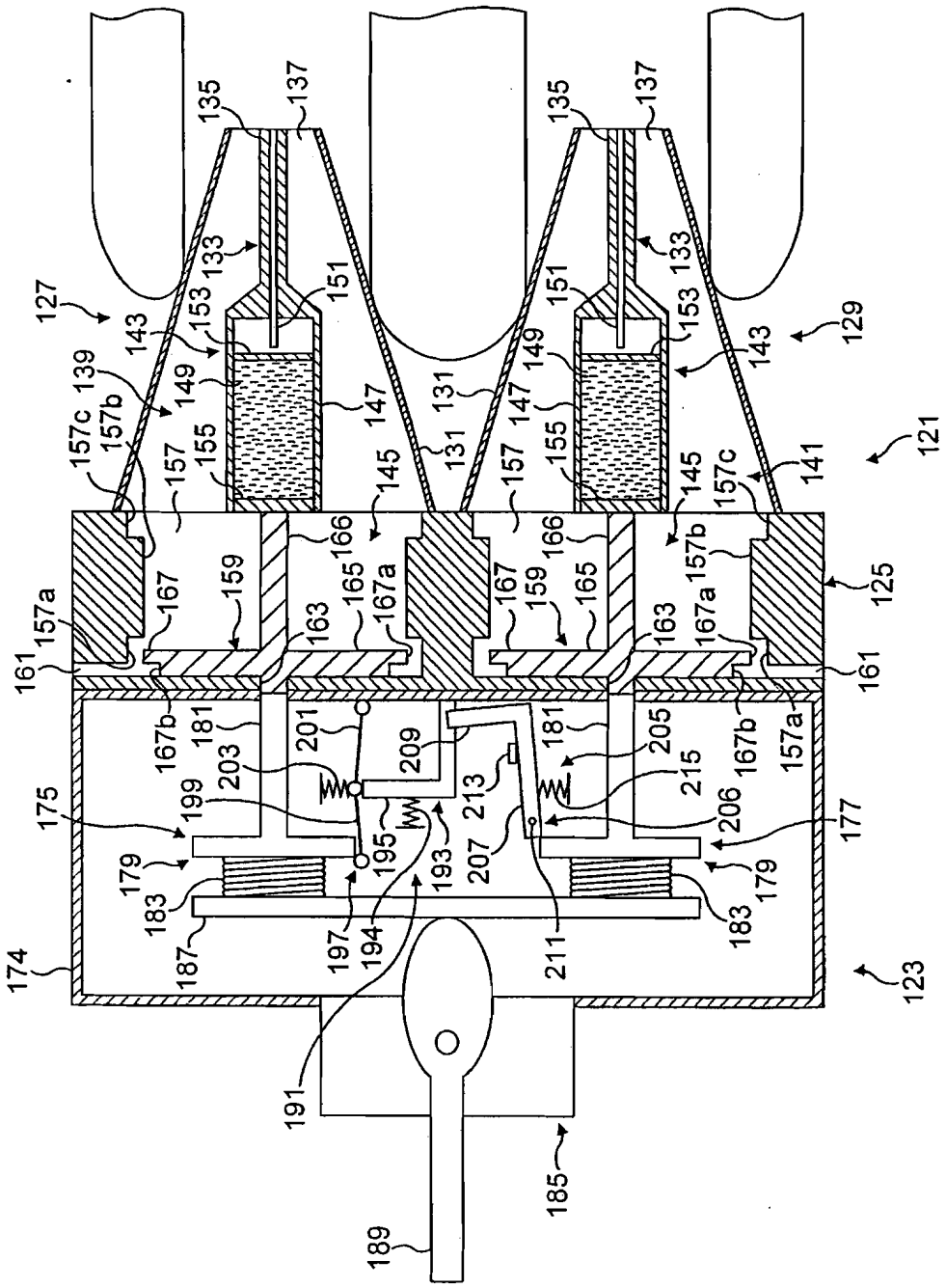
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FIG. 12(a)

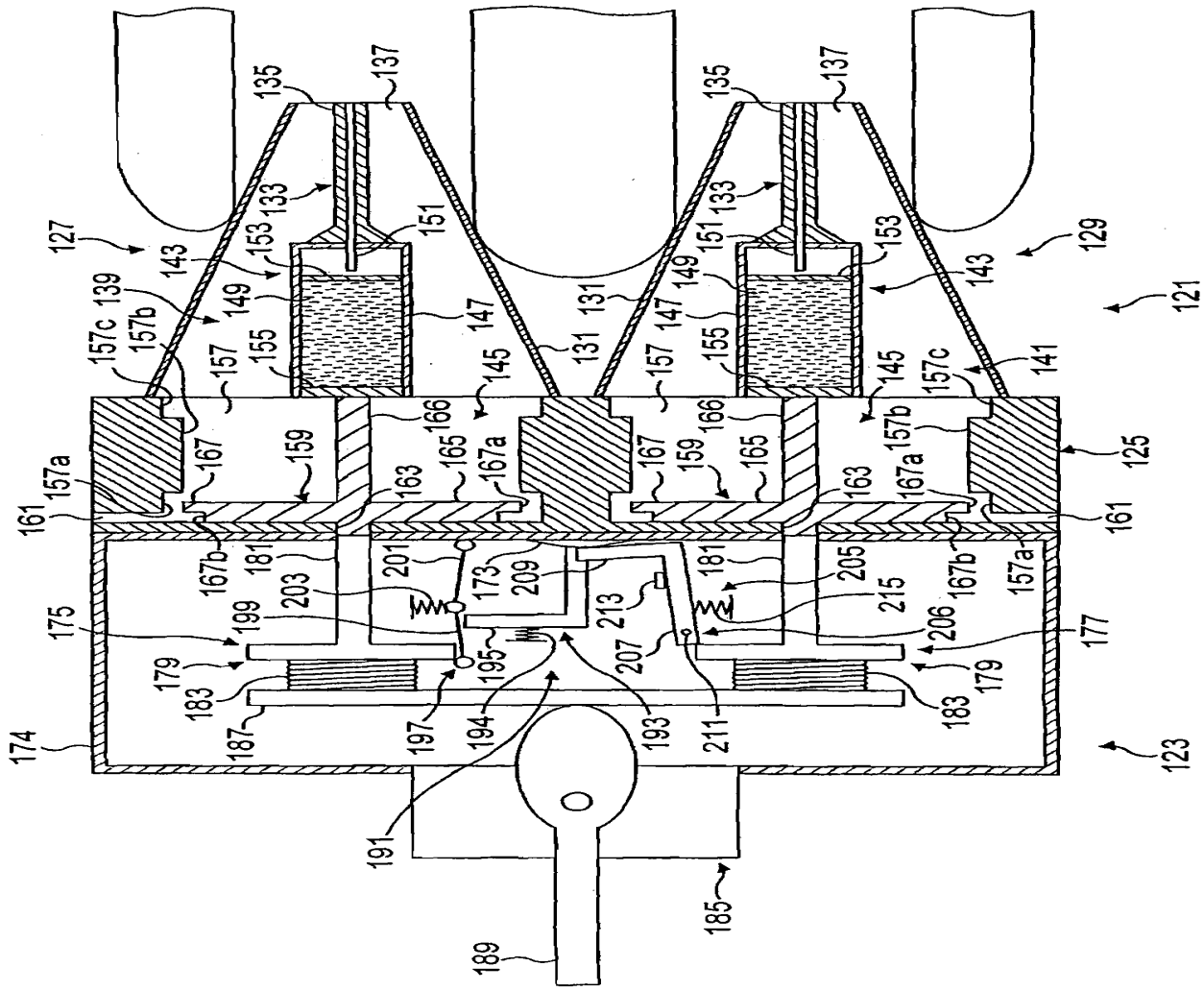
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FIG. 12(b)

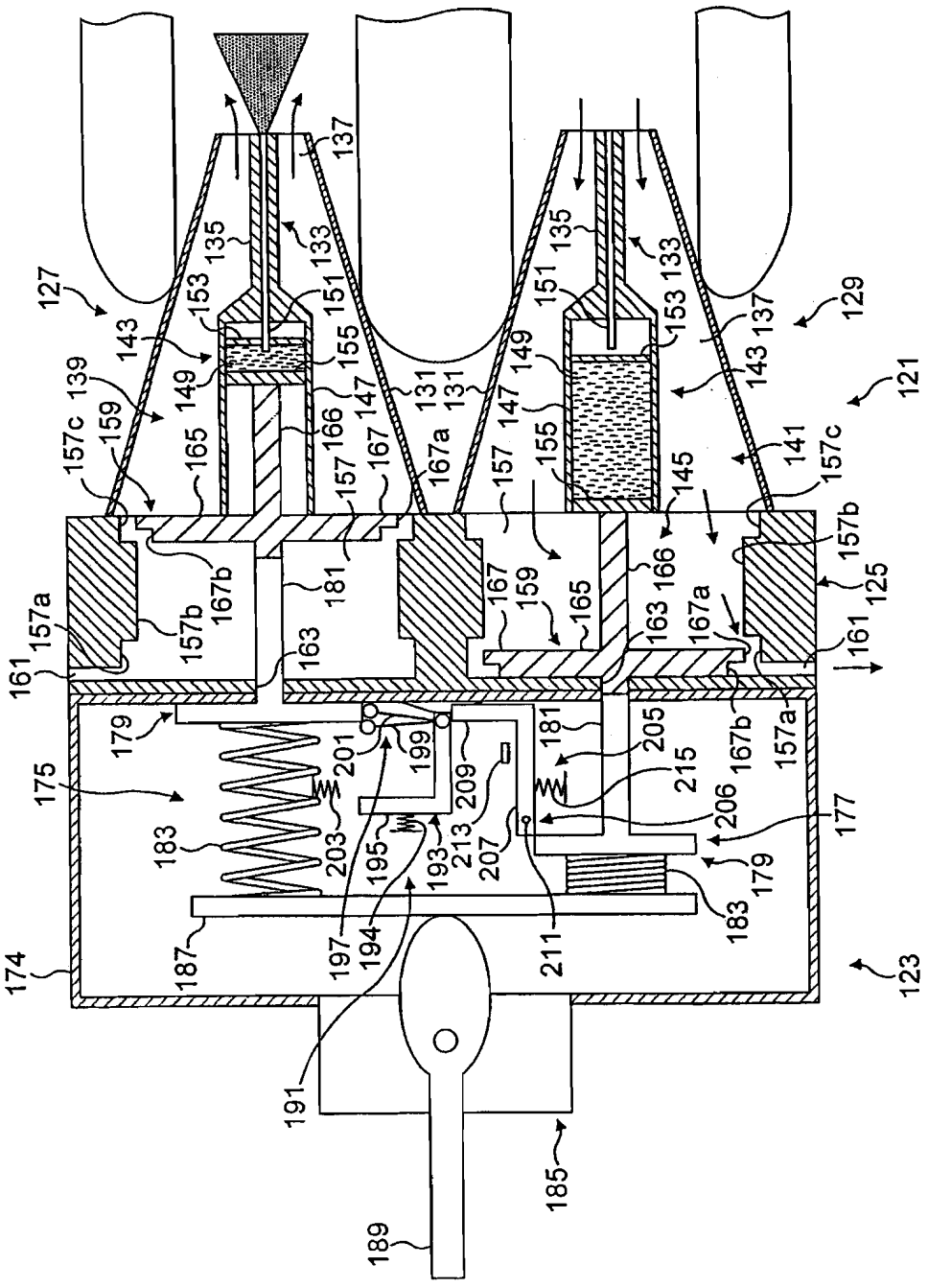
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FIG. 12(c)

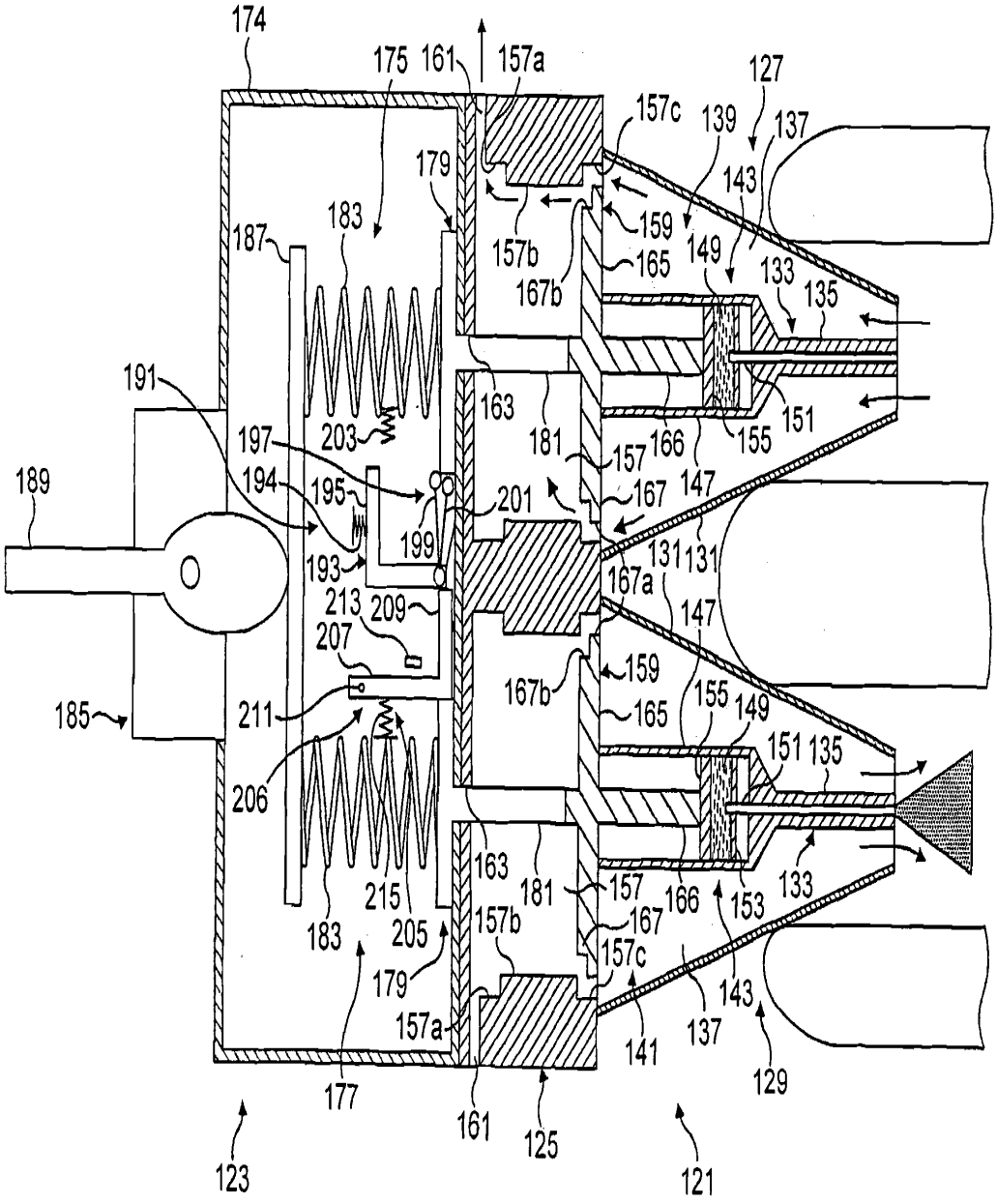
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FIG. 12(d)

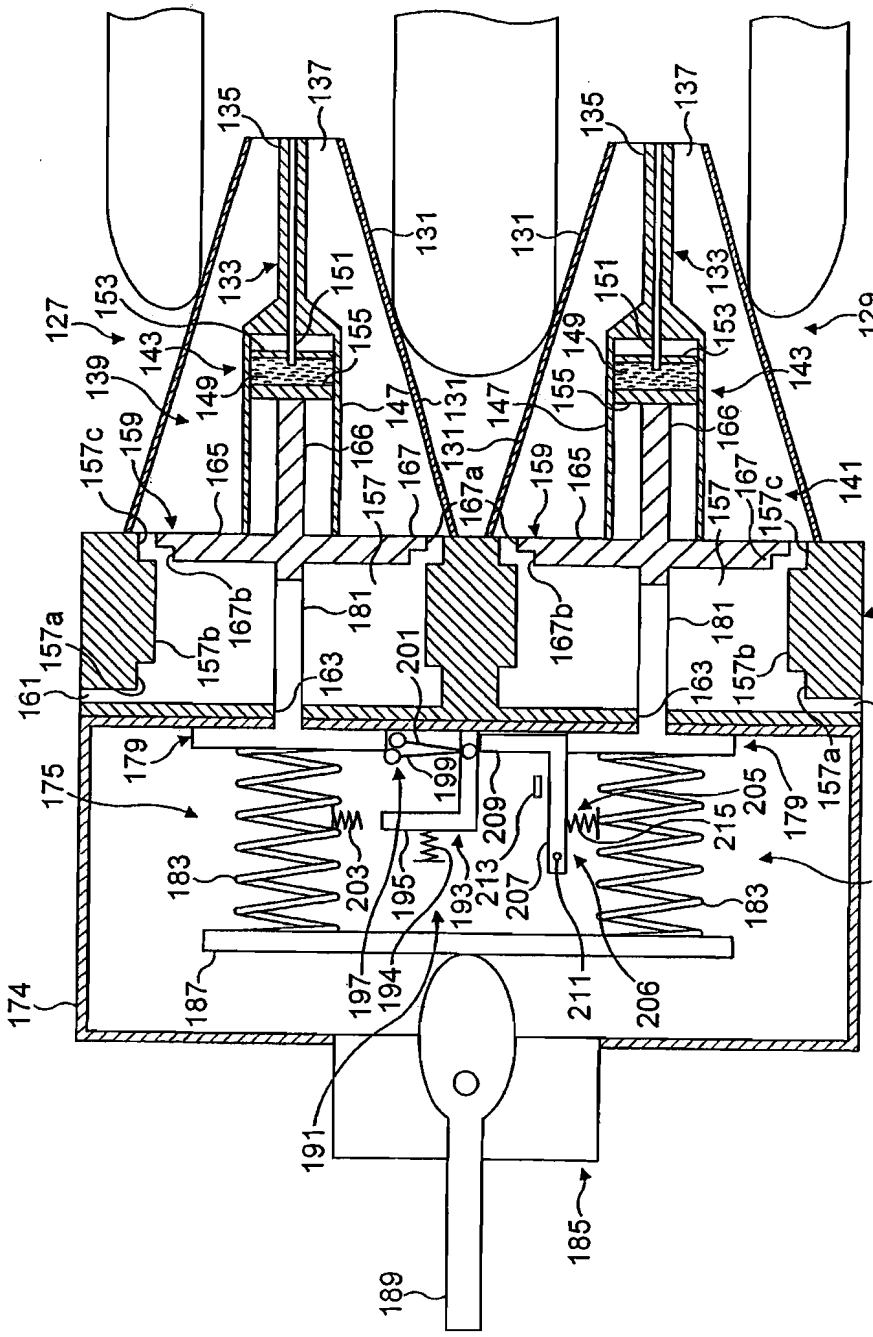
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FIG. 12(e)

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(75) Inventor/Applicant (*for US only*): **DJUPESLAND, Per, Gisle** [NO/NO]; Lokkaskogen 18C, N-0773 Oslo (NO).

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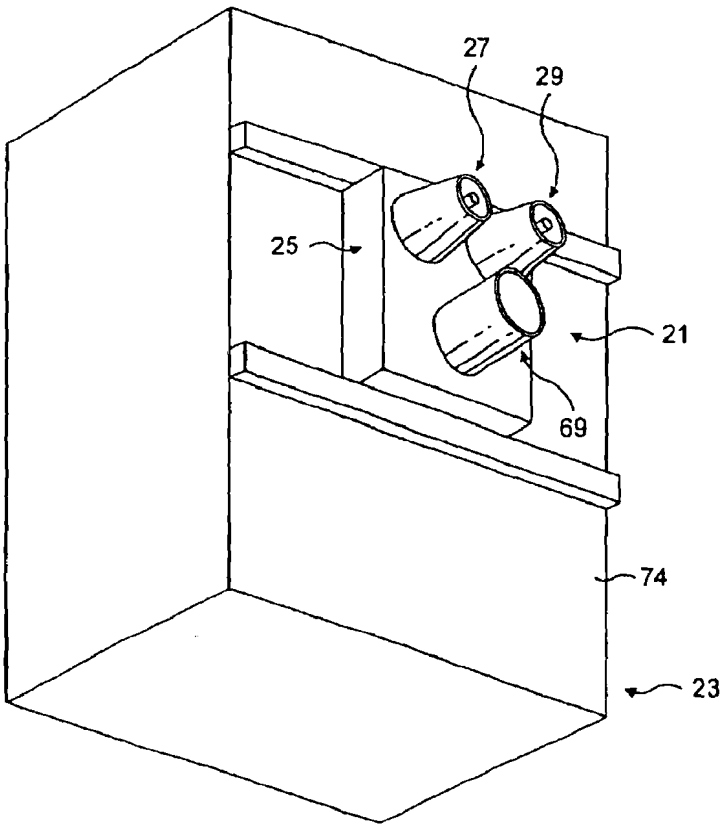
Published:
— *with international search report*

[Continued on next page]

(54) Title: NASAL DEVICES



(57) Abstract: A nasal delivery device for and a method of delivering substance to a nasal airway of a subject, in particular in the mass treatment, especially mass vaccination, of subjects, the delivery device comprising: an interface unit, as a replaceable unit, including at least one nosepiece unit for fitting to a respective nostril of a subject and including a nozzle from which substance is in use delivered, and at least one delivery unit including a substance supply unit for delivering substance to the nozzle of the at least one nosepiece unit; and an actuation unit for actuating the at least one delivery unit of the interface unit.

WO 2004/004814 A3

(88) Date of publication of the international search report:
21 May 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/03274

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/08 //A61M11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 779 078 A (DOTT LTD COMP ;ATSUGI UNISIA CORP (JP)) 18 June 1997 (1997-06-18) column 12, line 24 - line 42; figures 7,8 ---	1-3,12, 14-16, 52,53, 62,67, 76,77
X	EP 1 180 378 A (OPTINOSE AS) 20 February 2002 (2002-02-20) claims 1-19; figures 4-9 --- -/--	1-3, 10-12, 14-23, 52,53, 60-62, 67-77

[X] Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
24 November 2003	21 JAN. 2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer LEIF BRANDER / ELY

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 03/03274

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 26-51
because they relate to subject matter not required to be searched by this Authority, namely:

Methods for treatment of the human or animal body by surgery or therapy (PCT Rule 39.1(iv)).

2. [X] Claims Nos.: 82-85
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 82-85

Claims shall not rely on references to the description or drawings (PCT Rule 6.2(a)).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Interna ..l Application No
PCT/IB 03/03274

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
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(19) Europäisches Patentamt
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Office européen des brevets

(11) EP 0 779 078 A1

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(51) Int. Cl.[6]: **A61M 15/08**

(86) International application number:
PCT/JP96/01798

(87) International publication number:
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(84) Designated Contracting States:
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(30) Priority: **30.06.1995 JP 188534/95**
11.08.1995 JP 227265/95

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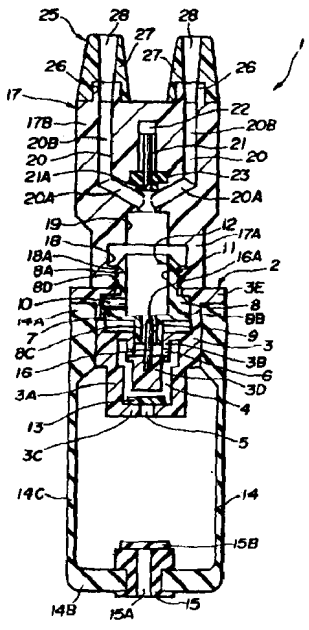
(54) NASAL CAVITY MEDICATOR AND METHOD OF USING SAME

(57) A distance-adjustable nozzle mechanism 25 is disposed to a passage member 17 to be located at the ejection sides of left and right medicine passages 20, 20. The distance-adjustable nozzle distance 25 includes fitting projection sections 26, 26 formed in the passage member 17, adjustable nozzles 27, 27 which are rotatably and detachably attached to the fitting projection sections 26, and tapered spray holes 28 each of which is in communication with the medicine passage 20 and formed throughout the fitting projection section 26 and the adjustable nozzle 27, in which the axis of the adjustable nozzle 27 is eccentric to a rotational center. Accordingly, when each adjustable nozzle 27 is rotated, the nozzles can approach to or separate from each other by an amount corresponding to the eccentricity relative to the rotational center, so that the nozzle pitch between the respective adjustable nozzles 27 can be easily adjusted in conformity with the distance between the nasal cavities of the patient. Additionally, cleaning can be facilitated by removing each adjustable nozzle 27.

FIG.2



EP 0 779 078 A1

Description

FIELD OF THE INVENTION

The present invention relates to a medicine administering device suitable for administering powder-state medicine filled in a medicine accommodating chamber, to nasal cavities, and a method of using the same.

BACKGROUND TECHNIQUE

In general, a method of curing by administering powder-state medicine through nasal cavities have been employed for a patient of nasal allergy, asthma and the like. In this curing method, the powder-state medicine filled in a medicine accommodating chamber such as a capsule or the like is administered into nasal cavities by using an exclusive medicine administering device for nasal cavities.

As a sprayer to be used for this curing method, one shown in Japanese Patent Provisional Publication No. 59-34267 has been known.

In the sprayer according to this conventional technique, a cylindrical member is provided at its air inflow-side with a pump section and is formed at its air outflow-side with a concave-shaped section into which a capsule is to be inserted. The cylindrical member is detachably provided at its tip end side with a tip end section which is formed with an opening section which serves as a medicine spray hole, in which the tip end section is fitted to the cylindrical member to form a capsule accommodating section inside them. Further, a cap is provided to be detachably fitted throughout the above-mentioned cylindrical member and the tip end section, and the capsule is provided thereinside with an axially extending needle. The cap is fitted to the above-mentioned cylindrical member thereby forming a hole in the capsule accommodated in the capsule accommodating section with the needle inside the cap.

In the thus arranged conventional technique, first when the hole is formed in the capsule for the purpose of making preparation of medicine administration, the capsule filled with powder-like medicine is inserted in the concave-shaped section of the cylindrical member. Thereafter, the tip end section is fitted to the cylindrical member thereby accommodating the capsule in the capsule accommodating section. Then, the cap is installed through the tip end section in such a manner that the needle pierces the opening section of the tip end section of the tip end section, thereby forming holes at the axially opposite sides of the capsule under the action of the needle disposed inside the cap.

Next, when the medicine is administered, the tip end section is inserted into one of the nasal cavities of the patient upon detaching the cap from the cylindrical member. Then, the pump section is pressed so that air from the pump section is flown through an air introduction passage into the capsule. Accordingly, the medicine in the capsule is sprayed through the opening section into the nasal cavities of the patient under the action of this air. Insertion of the tip end section into the nasal cavity is made alternately to the both nasal cavities upon repeating the pressing action of the pump section thereby accomplishing medicine administration to the patient.

Additionally, a clearance is formed between the capsule accommodating section and the capsule in order that the medicine administration to nasal cavities is made alternately to the left and right nasal cavities so as to prevent the whole medicine in the capsule from being administered under only one pressing action of the pump section, in which a predetermined amount of the medicine is administered under about four times of the pressing actions of the pump section for each nasal cavity.

Now, in the sprayer according to the above-discussed conventional technique, medicine administration is made for one by one of the left and right nasal cavities, and therefore the pressing action of the pump section and the insertion of the cylindrical member into the nasal cavity is required to be repeated many times in order to supply the left and right nasal cavities with an equal amount of the medicine. Accordingly, there is a problem that treatment during medicine administration becomes troublesome.

Furthermore, when the hole is formed in the capsule in order to make preparation of the medicine administration, the tip end section is detached from the cylindrical member, and then the capsule is accommodated. Under this state, the cap is fitted around the above-mentioned cylindrical member and the tip end section thereby accomplishing the hole formation. When the medicine is to be sprayed, the pump section is operated to accomplish the spraying into the nasal cavities after the cap is again detached. Accordingly, it is required to install and detach the cap, thereby providing such problems that not only the preparation action is troublesome but also there is the fear of losing the cap.

Furthermore, even if a medicine administering device provided with left and right medicine spraying openings is produced, there is a problem that it is required to prepare a plurality of kinds of the devices which are different in distance between the nasal cavities because the distance between the nasal cavities is personally different among, for example, children and adults.

The present invention has been made in view of the above-discussed problems of the conventional technique and be intended to provide a medicine administering device for nasal cavities which device can administer the medicine in the medicine accommodating chamber simultaneously into the left and right nasal cavities of the patient under simple operations and be extensively used throughout children and adults.

DISCLOSURE OF THE INVENTION

A medicine administering device for nasal cavities,

of the present invention is arranged basically such that a separation-distance between left and right nozzles in left and right directions is adjustable in conformity with a distance between left and right nasal cavities of a patient when powder-like medicine within a medicine accommodating chamber is sprayed from the left and right nozzles respectively into the left and right nasal cavities of the patient under a condition where the powder-like medicine has been accommodated in the medicine accommodating chamber.

Accordingly, when the medicine within the medicine accommodating chamber is sprayed from the left and right nozzles respectively into the left and right nasal cavities of the patient, the separation-distance between the nozzle in the left and right directions can be adjusted in conformity with the distance between the nasal cavities of the patient, thereby making it possible to insert the left and right nozzles into the desired positions within the nasal cavities.

Additionally, the present invention comprises a medicine accommodating chamber accommodating therein powder-like medicine, air supply means for supplying air toward the medicine accommodating chamber, passage means including left and right medicine passages through which the medicine in the medicine accommodating chamber is supplied toward left and right nasal cavities of a patient by air supplied from the air supply means, and distance-adjustable nozzle means disposed at ejection side of the medicine passage of the passage means and adjustable in conformity with a distance between the nasal cavities of the patient in order to spray the medicine under a condition to be inserted into the left and right nasal cavities of the patient.

Accordingly, when air is supplied from the air supply means toward the medicine accommodating chamber under the condition where the medicine has been accommodated within the medicine accommodating chamber, the medicine within the medicine accommodating chamber is simultaneously sprayed to the left and right nasal cavities of the patient from the left and right medicine passages constituting the passage means upon being stirred under the action of air from the air supply means. Additionally, when the distance-adjustable nozzle means is inserted into the left and right nasal cavities of the patient, the distance-adjustable nozzle means is adjusted in conformity with the distance between the left and right nasal cavities of the patient, thereby making it possible to securely inserting the distance-adjustable nozzle means into the desired position of the nasal cavity.

Furthermore, the present invention comprises a medicine accommodating chamber accommodating therein powder-like medicine, air supply means for supplying air toward the medicine accommodating chamber, passage means including left and right medicine passages through which the medicine in the medicine accommodating chamber is supplied toward left and right nasal cavities of a patient by air supplied from the air supply means, and distance-adjustable nozzle means including left and right nozzles disposed respectively at ejection sides of medicine passages of the above-mentioned passage means in order to spray the medicine under a state to be inserted respectively in the left and right nasal cavities of the patient, wherein at least one nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is disposed rotatable, and the above-mentioned nozzle is disposed at a position eccentric to a rotational center.

Accordingly, when air is supplied from the air supply means toward the medicine accommodating chamber under the condition where the medicine has been accommodated within the medicine accommodating chamber, the medicine within the medicine accommodating chamber is simultaneously sprayed to the left and right nasal cavities of the patient from the left and right medicine passages constituting the passage means upon being stirred under the action of air from the air supply means. Additionally, when the rotatably disposed nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is rotated, the nozzle turns with a radius corresponding to an eccentric amount. Therefore, by adjusting a rotational amount at this time, the distance between the left and right nozzles is brought into conformity with the distance between the nasal cavities of the patient.

Additionally, the present invention is arranged such that at least one nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is disposed detachable to the above-mentioned passage means.

Accordingly, the respective nozzles and the medicine passages can be sufficiently and easily cleaned by detaching the left and right nozzles from the passage means.

Furthermore, the present invention is arranged such that a spray hole of the nozzle constituting the above-mentioned distance-adjustable nozzle means is formed generally straight.

Accordingly, when the medicine within the medicine accommodating chamber is sprayed into the left and right nasal cavities of the patient, air containing the medicine straight flows from the left and right medicine passages toward the spray holes, so that the air is sprayed into the nasal cavities under its condition to be provided with straightened flow characteristic and straight advancing characteristic.

Further, the present invention is arranged such that a spray hole of the nozzle constituting the above-mentioned distance-adjustable nozzle means is formed eccentric.

Accordingly, when the left and right nozzles constituting the distance-adjustable nozzle means are rotated, the eccentric spray holes are rotationally moved together with the respective nozzles, and therefore the spray hole can be positioned at the center of the nasal cavity when the each nozzle is inserted into the nasal cavity, so that the medicine can be uniformly sprayed

cavities, according to the third embodiment of the present invention; Fig. 16 is a cross-sectional view showing a condition where an adjustable nozzle is fitted to a left and right direction guide groove and to a nozzle holding projection section, as seen from a direction indicated by an arrow XVI-XVI in Fig. 15; Fig. 17 is an enlarged sectional view of an essential part, showing a condition where the adjustable nozzles are most separated from each other in the left and right directions; Fig. 18 is an enlarged sectional view of an essential part, showing a condition where the adjustable nozzles are most approached to each other in the left and right directions; and Fig. 19 is a cross-sectional view showing the distance-adjustable nozzle mechanism according to a modified example of the third embodiment.

THE BEST MODE FOR CARRYING OUT THE INVENTION

Hereinafter, a medicine administering device for nasal cavities, according to embodiments of the present invention will be discussed with reference to Fig. 1 to Fig. 18.

First, a first embodiment of the present invention is shown in Fig. 1 to Fig. 8.

In the drawings, the reference numeral 1 designates the medicine administering device for nasal cavities, according to this embodiment. The medicine administering device 1 for nasal cavities generally comprises a capsule holder 2 discussed after, a pump section 14, a medicine passage 20, and a distance-adjustable nozzle mechanism 25 as shown in Fig. 2.

The above-mentioned capsule holder 2 is arranged to hold a capsule and includes a stationary member 3 which is formed into the double-cylinder shape and will be discussed after, and a movable member 8 which is located at the inner peripheral side of the stationary member 3 and disposed to be axially movable relative to the stationary member 3.

The above-mentioned stationary member 3 generally includes an outer cylindrical section 3A which is formed into the shape of a cylinder with a step, an inner cylindrical section 3B formed inside the outer cylindrical section 3A, a bottom section 3C for closing the lower end side of the above-mentioned outer cylindrical section 3A, a medicine trapping section 3D forming a bottom section of the above-mentioned inner cylindrical section 3B, and a flange section 3E formed to be located at the opening side of the above-mentioned outer cylindrical section 3A. The flange section 3E is arranged to prevent the movable member 8, axially movable along the inner peripheral surface of the outer cylindrical section 3A, from coming out and to locate a pump section 14 which is disposed to cover the stationary member 3 from the outer peripheral side. The outer cylindrical section 3A and the inner cylindrical section 3B are arranged such that an opening section of the inner cylindrical section 3B is connected to the outer cylindrical section 3A at the axial intermediate portion so that an air inflow chamber 4 is formed between the cylindrical sections 3A, 3B.

The bottom section 3C of the above-mentioned stationary member 3 is formed with an air supply passage 5 which is in communication with the above-mentioned air inflow chamber 4. The medicine trapping section 3D serving as the bottom section of the inner cylindrical section 3B is provided with a first perforating pin 16 which will be discussed after and is formed projecting toward the side of a one-side capsule hole 11. The inner cylindrical section 3B is formed with communication holes 6, 6 through which the inner peripheral side thereof and the air inflow chamber 4 are in communication with each other, and the outer cylindrical section 3A is formed at its inner peripheral surface with an engaging groove 7 which axially extends to be engagable with a rotation-preventing pin 10 which will be discussed after.

The above-mentioned movable member 8 is disposed axially movable inside the outer-cylindrical section 3A of the stationary member 3, and includes a cylindrical section 8A, a large-diameter bottom section 8B which is disposed at the lower end side of the cylindrical section 8A and axially movably held inside the above-mentioned outer cylindrical section 3A, and a small-diameter projecting section which extends from the central portion of the bottom section 8B into the inner cylindrical section 3B. The cylindrical section 8C is formed with a pin insertion hole 9 which extends in the axial direction thereof and pierces the bottom section 8B to be in communication with the inside of the cylindrical section 8A, in which the first perforating pin 16 passes through the pin insertion hole 9. The cylindrical section 8A is provided at its outer peripheral side with the rotation-preventing pin 10 which is formed projecting radially outwardly. The rotation-preventing pin 10 is to be brought into engagement with the engaging groove 7 of the stationary member 3 thereby allowing the movable member 8 to axially move relative to stationary member 3 and restricting the rotation of the movable member 8 relative to the stationary member 3.

The inner peripheral side of the cylindrical section 8A of the above-mentioned movable member 8 serves as the one-side capsule hole 11 which is incorporated with the other-side capsule hole 19 to constitute a capsule accommodating hole 12 which serves as a medicine accommodating chamber.

Thus, in the capsule holder 2 according to this embodiment, the movable member 8 is arranged to be axially movable along the outer cylindrical section 3A of the stationary member 3. Additionally, when an external thread 8D of the movable member 8 is brought into engagement with an internal thread 18A which will be discussed after, the movable member 8 is automatically raised to the side of a passage member 17 because the rotation of the movable member 8 relative to the stationary member 3 is restricted by the rotation-preventing pin 10.

The reference numeral 13 designates a supply

valve disposed inside the air inflow chamber 4. The supply valve 13 is arranged to open and close the air supply passage 5 formed in the stationary member 3, and arranged to make an valve-opening when air is supplied from the pump section 14 and to be seated to close the air supply passage 5 when air is sucked into the pump section 14.

The reference numeral 14 designates a pump section which is formed of a rubber material and formed into the shape of a cylinder with a bottom to serve as air supply means. The pump section 14 includes a thick-wall opening section 14A, a bottom section 14B, and a pressing section 14C located between the opening section 14A and the bottom section 14B. The above-mentioned opening section 14A is installed to the outer cylindrical section 3A of the stationary member 3 to maintain a gas tight seal. Almost all parts of the capsule holder 2 are accommodated inside the pump section 14, by which the medicine administering device 1 for nasal cavities is axially small-sized.

The reference numeral 15 designates a suction valve disposed at the bottom section 14B of the pump section 14. The suction valve 15 generally includes a suction passage 15A which is located at the central portion thereof and in communication with the inside of the pump section 14, and a valve member 15B which opens and closes the suction passage 15A. The valve member 15B makes a valve opening when air is supplied from the pump section 14, and makes a valve closing when air is sucked from the outside into the pump section 14.

The reference numeral 16 designates the first perforating pin provided to the stationary member 3. The first perforating pin 16 has a base end side which is fixed to the medicine trapping section 3D, and a tip end side which is formed into a sharp needle end 16A. The first perforating pin 16 is arranged such that the needle end 16A is projected into the one-side capsule hole 11 when the movable member 8 is located at the side of the pump section 14. Thrusting a capsule K into the one-side capsule hole 11 under this state can form an air inflow hole H1 in the capsule K. When the movable member 8 is located at the side of the passage member 17, the needle end 16A is withdrawn into the pin insertion hole 9, and therefore the needle end 16A is brought into a state to have been extracted from the air inflow hole H1.

The reference numeral 17 designates the passage member which is threaded to the movable member and serves as passage means. The passage member 17 has a one side which is located at the side of the capsule holder 2 forms a small-diameter section 17A, and the other side which forms a large-diameter section 17B. The large-diameter section 17B is provided with the left and right distance-adjustable nozzle mechanism 25.

A movable member threaded hole 18 is formed in the above-mentioned small-diameter section 17A . An internal thread 18A to be engaged with an external thread 8D of the movable member 8 is formed at the inner periphery at the opening side of the movable member threading hole 18. The other-side capsule hole 19 is formed at the innermost part of the movable member threading hole18, the capsule hole 19 constituting the capsule accommodating hole 12, in cooperation with the one-side capsule hole 11.

The reference numerals 20, 20 designate respectively left and right medicine passages formed in the passage member 17. Each medicine passage 20 includes a branched passage 20A which is in communication with the other-side capsule hole 19 and branched off, and a straight passage section 20B which axially extends from the bifurcated passage 20A, so that the medicine passages are formed generally U-shaped. Each straight passage section 20B is formed at its ejection side into a tapered spray hole 28 which will be discussed after, as shown also in Fig. 3.

The reference numeral 21 designates a second perforating pin which is disposed to be opposite to the first perforating pin 16. The second perforating pin 21 has a base end side which is fixed to a slidable block 22 which is disposed to be axially slidable, and a tip end side which extends to pierce a seal rubber 23 and has a tip end which is formed into a sharp needle end 21A. The above-mentioned slidable block 22 is connected to an operation plate 24 (See Fig. 1) disposed outside the passage member 17 to operate the second perforating pin 21. The second perforating pin 21 is arranged to be moved through the slidable block 22 in the direction indicated by an arrow A by moving the operation plate 24 in a direction indicated by the arrow A, in which an air outflow hole H2 is formed in the capsule K with the needle end 21A of the pin 21.

The reference numeral 25 designates the distance-adjustable nozzle mechanism disposed to the passage member 17. The distance-adjustable nozzle mechanism 25 includes left and right fitting projection sections 26, 26 which are disposed at the side of the passage member 17 and will be discussed after, left and right adjustable nozzles 27, 27 each of which is rotatably installed to each fitting projection section 26, and tapered spray holes 28, 28 each of which is formed throughout each adjustable nozzle 27 and each fitting projection section 26.

The reference numerals 26, 26 designate respectively the left and right fitting projection sections disposed at the upper end surface side of the passage member 17. Each fitting projection 26 is formed into the shape of a cylinder integrally projected from the passage member 17 to cover the ejection side of the straight passage section 20B of the left or right medicine passage 20.

The reference numerals 27, 27 designate respectively the left and right adjustable nozzles which are respectively detachably installed to the fitting projection sections 26, 26. Each adjustable nozzle 27 is to be inserted into the nasal cavity of the patient and formed into the frustoconical shape so that the diameter thereof gradually decreases toward the tip end side of the noz-

zle 27. The inner periphery of the base end side of the each adjustable nozzle 27 is formed as a fitting hole section 27A which is rotatably and detachably fitted to each fitting projection section 26. Each adjustable nozzle 27 is rotated relative to each fitting projection 26 thereby adjusting a nozzle pitch in conformity with a distance between nasal cavities of the patient for the reasons discussed below.

The reference numerals 28, 28 designate respectively tapered spray holes each of which is formed throughout the inner periphery of each fitting projection 26 and the inner periphery of each adjustable nozzle 27 and gradually spread toward the tip end side. Each tapered spray hole 28 is disposed coaxial with the straight passage section 20B of each medicine passage 20. Each tapered spray hole 28 is arranged such that when air containing the medicine is supplied from each medicine passage 20, this air containing the medicine is flown to gradually spread in a manner to move along the tapered inner wall surface, so that the medicine is administered in a spread manner into the nasal cavities.

The thus arranged adjustable nozzle mechanism 25 is configured such that each adjustable nozzle 27 is disposed rotatable around an axis C1 (as a rotational center) of the straight passage section 20B of the medicine passage 20 and the tapered spray hole 28 as shown in Fig. 3, in which each adjustable nozzle 27 has an axis C2 which is eccentric to or separate from the axis C1 as the rotational center by an eccentric amount d1. Accordingly, by rotating each adjustable nozzle 27, the nozzle pitch between the respective adjustable nozzles 27 becomes L1 at a maximum-separated state as shown in Figs. 3 and 4, while the nozzle pitch between the respective adjustable nozzles 27 becomes L2 at a minimum and approaching state as shown in Figs. 5 and 6. As a result, by suitably adjusting the rotational amount of each adjustable nozzle 27, the nozzle pitch can be brought into conformity with the distance between the nasal cavities of the patient.

The medicine administering device for nasal cavities, according to this embodiment has the above-discussed arrangement. Next, its operation for use will be discussed.

First, the movable member 8 of the capsule holder 2 is located to the side of the pump section 14, so that the needle end 16A of the first perforating pun 16 is brought into a state to be projected into the one-side capsule hole 11. When the capsule K is thrust into the one-side capsule hole 11 in this state, the needle end 16A of the pin 16 is stuck into the capsule K, so that the air inflow hole H1 is formed in the capsule K (See Fig. 7).

Next, in order to assemble the passage member 17 to the capsule holder 2, the internal thread 18A at the side of the passage member 17 is threaded with the external thread 8D at the side of the capsule holder 2. By this, the movable member 8 of the capsule holder 2 moves toward the side of the passage member 17 upon screwing the passage member 17, and therefore the capsule K is maintained in a state to be slightly axially pressed within the capsule accommodating hole 12. At this time, the needle end 16A of the first perforating pin 16 which has formed the air inflow hole H1 in the capsule K is extracted, so that the inside of the capsule K is brought into communication with the air inflow chamber 4 through the pin insertion hole 9 and the respective communication holes 6.

Under this condition, in order to form the air outflow hole H2 in the capsule K, the operation plate 24 is moved in the direction indicated by the arrow A, and therefore the second perforating pin 21 is moved toward the capsule K so that air outflow hole H2 is formed in the capsule K with the needle end 21A of the second perforating pin 21. Thereafter, the operation plate 24 is returned to its original position so that the needle end 21A is extracted from the capsule K. By this, perforating as a medicine administration preparation has been accomplished.

Next, discussion will be made on a medicine administration operation for spraying into the nasal cavities of the patient the medicine within the capsule whose perforating has been completed.

First, the respective adjustable nozzles 27 are inserted into the both nasal cavities of the patient, and then the pressing section 14C of the pump section 14 is smashed as shown in Fig. 8 so that air stream is generated from the pump section 14. This air is acted to the air supply passage 5 so that the supply valve 13 is pressed against the medicine trapping section 3D of the inner cylindrical section 3B to make the valve-opening. Accordingly, the air is flown into the capsule K through the air inflow chamber 4, the respective communication holes 6, the pin insertion hole 9 and the air inflow hole H1. By this, the air flown into the capsule K stirs the medicine to become air in which the medicine is mixed. This air mixed with the medicine is sprayed from the left and right tapered spray holes 28, 28 through the air outflow hole H2 and the left and right medicine passages 20, 20, so that the medicine can be simultaneously administered into the left and right nasal cavities of the patient.

When the left and right adjustable nozzles 27 are inserted into the left and right nasal cavities of the patient in order to administer the medicine within the capsule K to the patient, each adjustable nozzle 27 is suitably rotated to suitably adjust the nozzle pitch within a range of from the nozzle pitch L1 for establishing the maximum-separated state and the nozzle pitch L2 for establishing the minimum and approaching state. As a result, the nozzle pitch between the respective adjustable nozzles 27 can be brought into conformity with the distance between the nasal cavities of the patient, so that the respective adjustable nozzles 27 can be inserted into desired positions in the nasal cavities of the patient securely and smoothly without a feeling of physical disorder.

Thus, according to this embodiment, the air inflow hole H1 and the air outflow hole H2 can be easily

formed axially in the capsule K upon an action of installing the capsule K to the movable member 8 and upon an action of once reciprocating axially the second perforating pin 21. As a result, the preparation action before the medicine administration action can be largely simplified, and the left and right nasal cavities of the patient can be simultaneously administered since the medicine within the capsule K is sprayed from the left and right adjustable nozzles 27, 27 through the left and right medicine passages 20, 20. Accordingly, treatment ability of the medicine administering device 1 for nasal cavities can be largely improved from the viewpoints of the preparation action and the medicine administration action.

Additionally, by rotating each adjustable nozzle 27 in order to insert the respective adjustable nozzles 27 into the nasal cavities of the patient, the nozzle pitch can be very easily brought into conformity with the distance between the nasal cavities within the range of from the nozzle pitch L1 for establishing the maximum-separated state and the nozzle pitch L2 for establishing the minimum and approaching state. As a result, each adjustable nozzle 27 can be securely inserted into the desired position within the nasal cavity, so that spray of the medicine into the nasal cavities can be made good thereby improving a medicine administration efficiency.

Thus, by causing the locations of the respective adjustable nozzles 27 to be in conformity with the distance of the nasal cavities of the patient, the respective adjustable nozzles 27 can be smoothly inserted into the nasal cavities without a feeling of physical disorder during insertion so that administration can be made under the best condition suitable for each person, while the medicine administering device 1 for nasal cavities, of only one kind can be used throughout children and adults which are different in distance between nasal cavities thereby largely broadening an application range of the medicine administrating device 1 for nasal cavities. Particularly in this embodiment, the adjustable nozzles 27, 27 are disposed respectively at the left- and right-sides, and therefore an adjusting range of the nozzle pitch can be enlarged thereby further broadening the application range.

Additionally, since each adjustable nozzle 27 is detachable relative to the passage member 17, each adjustable nozzle 27, the medicine passage 20 and the like can be sufficiently and easily cleaned by removing each adjustable nozzle 27 after the medicine administration, thereby achieving improvements in operationability during cleaning and from the sanitary view point.

In this embodiment, the straight passage section 20B of each medicine passage 20 is disposed coaxial with the tapered spray hole 28, and therefore air containing the medicine is straight flown through each medicine passage 20 and the tapered spray hole 28, so that this air containing the medicine is provided with straightened flow characteristics and straight advancing characteristics and brought into an accelerated condition. As a result, the medicine can be supplied to the innermost part of the nasal cavity.

Each medicine passage 20 is provided at its spraying side with each tapered spray hole 28, in which air containing the medicine is spread through each tapered spray hole 28. Accordingly, the medicine can be uniformly administered throughout a wide range of the inside of the nasal cavity of the patient, so that a spraying efficiency of the medicine can be improved thereby promoting absorption of the medicine to the human body thus improving effects due to medicine administration.

The medicine administrating device 1 itself houses therein a tool for perforating the capsule K, and therefore the medicine administrating action can be accomplishing without making any removal action. Accordingly, not only attaching and detaching actions for the perforating tool (required by the conventional technique) are omitted, but also there is no fear of losing the perforating tool thereby rendering treatment of the medicine administrating device further safe.

Further, the medicine dropped through the air inflow hole H1 of the capsule K can be trapped by the medicine trapping section 3D of the stationary member 3, and the medicine trapped by the medicine trapping section 3D is carried by air from the pump section 14 during the medicine administrating action and supplied together with the medicine within the capsule K into the left and right nasal cavities of the patient. As a result, the amount of the medicine to be left in the medicine administrating device 1 for nasal cavities can be reduced so as to securely administer a predetermined amount of the medicine filled within the capsule K to the patient while reducing the frequency of cleaning of the medicine administrating device 1 for nasal cavities.

Next, a second embodiment of the present invention is shown in Figs. 9 to 11. A feature of this embodiment resides in the fact that the spray hole of the adjustable nozzle is disposed eccentric relative to the rotational center. In this embodiment, the same reference numerals are assigned to the same constituent elements as those in the above-mentioned first embodiment thereby omitting explanation of them.

In the drawings, the reference numeral 31 designates a medicine administering device for nasal cavities, according to this embodiment. The reference numeral 32 designates a passage member of the medicine administering device 31 for nasal cavities. The passage member 32 includes a small-diameter section 32A and a large-diameter section 32B generally similarly to the passage member 17 discussed in the above-mentioned first embodiment. However, the passage member 32 is different from that of the first embodiment in a point that the large-diameter section 32B is formed at its upper surface side with fitting groove sections 34, 34 which will be discussed after.

The reference numeral 33 designates a distance-adjustable nozzle mechanism. The distance-adjustable nozzle mechanism 33 includes left and right fitting groove sections 34, 34 which are disposed at the side of

the passage member 32 and will be discussed after, adjustable nozzles 35, 35 which are respectively rotatably installed to the fitting groove sections 34, and spray holes 36, 36 which are respectively formed in the adjustable nozzles 35.

The reference numerals 34, 34 designate respectively the left and right fitting groove sections. Each fitting groove section 34 is formed at a position corresponding to the left or right medicine passage 20 and formed into the shape of a circular hole.

The reference numerals 35, 35 designate respectively the left and right adjustable nozzles according to this embodiment, installed in the left and right fitting groove sections 34, 34. Each adjustable nozzle 35 includes a nasal cavity inserting section 35A whose diameter gradually decreases at its tip end side to be inserted into the nasal cavity of the patient, and a fitting section 35B which is formed at the base end side of the nasal cavity inserting section 35A and detachably and rotatably fitted in the fitting groove section 34.

Here, the above-mentioned nasal cavity inserting section 35A is arranged to be rotatable around an axis C3 (as a rotational center) of the fitting section 35B. An axis C4 of the nasal cavity inserting section 35A is eccentric relative to or separate from the axis C3 (as the rotational center) by a displacement amount d2. By virtue of this, the nozzle pitch between the respective nasal cavity inserting sections 35A takes L3 at the maximum-separated state as shown in Fig. 10 and L4 at the minimum and approaching state as shown in Fig. 11, upon rotating each adjustable nozzle 35. As a result, the nozzle pitch can be brought into conformity with the distance between the nasal cavities of the patient by suitably adjusting the rotational amount of each adjustable nozzle 35.

The reference numerals 36, 36 designate respectively spray holes which are formed respectively in the adjustable nozzles 35 and formed bent to take the generally L-shape. Each spray hole 36 includes an inclined section 36A in communication with the straight passage section 20B of each medicine passage 20, and a tapered section 36B which is in communication with the inclined section 36A and formed coaxial with the nasal cavity inserting section 35A. With this arrangement, when each nasal cavity inserting section 35A is inserted into the nasal cavity, each spray hole36 is positioned at the central part of the inside of the nasal cavity so that the medicine can be uniformly sprayed into the nasal cavity. Additionally, when air containing the medicine is supplied through each medicine passage 20, each spray hole 36 is arranged such that this air containing the medicine is flown spreading gradually in a manner to move along the inner wall surface of the tapered section 36B, thereby spreading and administering the medicine into the nasal cavity.

Thus, also with the thus arranged this embodiment, it is a matter of course that the generally same effects as those in the above-mentioned first embodiment can be obtained. Particularly in this embodiment, the tapered section 36B of each spray hole 36 is located at the center of (or coaxial with) the nasal cavity inserting section 35A of the adjustable nozzle 35 to be inserted into the patient, so that the medicine can be uniformly sprayed into the nasal cavity through the tapered section 36B. As a result, absorption of the medicine inside the nasal cavity can be further promoted, thereby improving the effects of the medicine.

While the tapered spray hole 28 is formed throughout each fitting projection section 26 and the adjustable nozzle 27 in the above-mentioned first embodiment, the following arrangement may be, for example, employed: Spray cylinders 42, 42 are provided at the upper end surface of the passage member 17, in which adjustable nozzles 43, 43 are respectively rotatably and detachably installed to the outer peripheral sides of the spray cylinders 42 while tapered spray holes 44, 44 are respectively formed at the inner peripheral sides of the above-mentioned spray cylinders 42, like a distance-adjustable nozzle mechanism 41 shown as a modified example in Fig. 12.

Additionally, the spray hole 36' may be formed straight extending in each adjustable nozzle 35, like the distance-adjustable nozzle mechanism 33' shown as a modified example of the second embodiment in Fig. 13.

While the left and right adjustable nozzles 27, 35, 43 are provided in the above-mentioned first and second embodiments in which the nozzle pitch is adjusted by rotating each adjustable nozzle 27, 35, 43, the following arrangement may be employed: One of the left and right nozzles is a fixed nozzle while the other one is an adjustable nozzle thereby adjusting the nozzle pitch.

While each adjustable nozzle 27, 35, 43 is arranged to be detachable in the above-mentioned first and second embodiments, each adjustable nozzle may be rotatably fixed, in which each adjustable nozzle can be prevented from being lost.

Next, a third embodiment of the present invention is shown in Figs. 14 to 18. A feature of this embodiment resides in the fact that the nozzle is arranged to be movable in left and right directions. In this embodiment, the same reference numerals are assigned to the same constituent elements as those in the above-mentioned first embodiment thereby omitting explanation of them.

In the drawings, the reference numeral 51 designates a medicine administrating device for nasal cavities, according to this embodiment, and the reference numeral 52 designates a passage member as passage means of the medicine administrating device 51 for nasal cavities. The passage member 52 includes a small-diameter section 52A and a large-diameter section 52B generally similarly to the passage member 17 as discussed in the above-mentioned first embodiment. However, the passage member 52 according to this embodiment is different from the first conventional technique in a point that a distance-adjustable nozzle mechanism 56 which will be discussed after is provided in place of the distance-adjustable nozzle mechanism 25 according to the first embodiment.

The reference numerals 53, 54 designate respectively left and right medicine passages according to this embodiment, formed in the passage member 52. The left and right medicine passages 53, 54 includes respectively branched passages 53A ,54A which are branched off and in communication with the other-side capsule hole 19, straight passage sections 53B, 54B which axially straight extend respectively from the branched passage sections 53A, 54A, so as to be formed generally U-shaped, in which the ejection side of the left-side straight passage section 53B becomes a spray hole 55 within a fixed nozzle 57 which will be discussed after. Additionally, the right-side straight passage section 54B is short as compared with the left-side straight passage section 53B, and has an ejection side to which a connecting pipe 63 discussed after is connected.

The reference numeral 56 designates the distance-adjustable nozzle mechanism according to this embodiment, provided in the large-diameter section 52B of the passage member 52. The distance-adjustable nozzle mechanism 56 includes the fixed nozzle which will be discussed after, a left and right direction guide groove 58, a nozzle holding projection section 59, an adjustable nozzle 61, the connecting pipe 63 and the like.

The reference numeral 57 designates the fixed nozzle which is located at the ejection side of the left-side medicine passage 53 and projected from the large-diameter section 52 of the passage member 52. The fixed nozzle 57 is arranged to be inserted into the nasal cavity of the patient and formed into the frustoconical shape so that its diameter gradually decreases toward its tip end side.

The reference numeral 58 designates the left and right direction guide groove formed to open to the other end surface of the large-diameter section 52B of the passage member 52, serving as a left and right direction guide section. The left and right direction guide groove 58 is located on the extension of the straight passage section 54B of the right-side medicine passage 54 and formed into the shape of ellipse which radially elongates as shown in Fig. 15. The width dimension (the diametrical dimension between the circular arcs) of the left and right direction guide groove 58 is set slightly larger than the diametrical dimension of the adjustable nozzle 61. With this, the adjustable nozzle 61 is movably supported to be movable in the left and right directions (the directions indicated by the arrows B and C).

The reference numeral 59 represents a nozzle holding projection section which is disposed within the left and right direction guide groove 58 and serves as a nozzle holding section. The nozzle holding projection section 59 projects from the inner peripheral surface of the left and right direction guide groove 58 and formed ring-shaped as shown in Fig. 16. The nozzle holding projection section 59 is in engagement with the annular groove 61A of the adjustable nozzle 61 and arranged to allow the adjustable nozzle 61 within the left and right direction guide groove 58 and prevents the adjustable nozzle 61 from falling off.

The reference numeral 60 represents a connecting pipe moving space formed between the straight passage section 54B of the right-side medicine passage 54 and the left and right direction guide groove 58. The connecting pipe moving space 60 is arranged to allow the connecting pipe 63 to move in the left and right directions in accordance with movement of the adjustable nozzle 61.

The reference numeral 61 designates the adjustable nozzle formed projecting from the large-diameter section 52B of the passage member 52. The adjustable nozzle 61 and the fixed nozzle 57 constitute a pair, in which the adjustable nozzle 61 is formed into the frustoconical shape so that its diameter gradually decreases toward its tip end side, generally similarly to the fixed nozzle 57. Additionally, the adjustable nozzle 61 is formed at the outer periphery of its base end side with the annular groove 61A which extends throughout the whole periphery thereof. The adjustable nozzle 61 is in engagement with the nozzle holding projection 59 through the annular groove 61A in a manner to be movable in the left and right directions.

The reference numeral 62 designates the spray hole formed in the adjustable nozzle 61. The spray hole 62 is located at the center of the adjustable nozzle 61 and formed to axially pierce the adjustable nozzle. Additionally, the spray hole 62 is in communication with the right-side medicine passage 54 through the connecting pipe 63.

The reference numeral 63 designates the connecting pipe disposed within the connecting pipe moving space 60. The connecting pipe 63 has a one-end side which is connected to the passage member 17 so as to be in communication with the straight passage section 54B of the right-side medicine passage 54, and the other-end side which is connected to the adjustable nozzle 61 so as to be in communication with the spray hole 62. Additionally, the connecting pipe 63 is made of plastic (resin) material or the like which has a sufficient flexibility. With this, when the adjustable nozzle 61 moves, the connecting pipe 63 deforms in accordance with the amount of movement of the adjustable nozzle thereby making it possible to always establish communication between the medicine passage 54 and the spray hole 62.

The thus arranged distance-adjustable nozzle mechanism 56 is configured such that the separation-distance (or the nozzle pitch) in the left and right directions of the adjustable nozzle 61 and the fixed nozzle 57 can be L5 for establishing the maximum-separated state by moving the adjustable nozzle 61 in the direction indicated by the arrow B as shown in Fig. 17, while the nozzle pitch can be L6 for establishing the minimum and approaching state by moving the adjustable nozzle 61 in the direction indicated by the arrow C as shown in Fig. 18. Accordingly, the nozzle pitch between the fixed nozzle 57 and the adjustable nozzle 61 can be brought into conformity with the distance between the nasal cavities

of the patient by moving the adjustable nozzle 61 in the directions indicated by the arrows B and C and by suitably adjusting the nozzle pitch within a range of from L5 for the maximum-separated state to L6 for the minimum and approaching state. Since the adjustable nozzle 61 is installed within the left and right direction guide groove 58 so that the annular groove 61A is in engagement with the nozzle holding projection section 59, the adjustable nozzle 61 can be prevented from falling off from the passage member 17.

Thus, also with the thus arranged embodiment, the generally same effects as those in the above-mentioned respective embodiments can be obtained. Particularly in this embodiment, by moving the adjustable nozzle 61 in the left and right directions along the left and right direction guide groove 58, the separation-distance (or the nozzle pitch) in the left and right directions of the adjustable nozzle 61 and the fixed nozzle 57 can be brought into conformity with the distance between the nasal cavities of the patient within the range of from L5 for the maximum-separated state to L6 for the minimum and approaching state, thereby further facilitating adjustment of the nozzle pitch.

Additionally, the nozzle holding projection section 59 is formed within the direction guide groove 58, in which the nozzle holding projection section 59 is in engagement with the annular groove 61A of the adjustable nozzle 61. As a result, the adjustable nozzle 61 can smoothly move along the nozzle holding projection section 59, and the adjustable nozzle 61 can be prevented from falling off from the passage member 52.

Further, the right-side medicine passage 54 and the spray hole 62 are in communication with each other through the connecting pipe 63 made of the flexible material, and therefore the medicine passage 54 and the spray hole 62 can be always in communication with each other, so that the medicine can be securely sprayed from the spray hole 62 toward the inside of the nasal cavities.

In the above-mentioned third embodiment, exemplification has been made on the distance-adjustable nozzle mechanism arranged such that the left-side one of the left and right nozzles is the fixed nozzle while the right-side one is the adjustable nozzle 61, so that the adjustable nozzle 61 is configured to be approached or separated relative to the fixed nozzle 57 thereby adjusting the nozzle pitch. However, the distance-adjustable nozzle mechanism 56 may arranged for example such that, like a distance-adjustable nozzle mechanism 71 shown as a modified example in Fig. 19, left and right direction guide grooves 72, 72, nozzle holding projection sections 73, 73, and connecting pipe moving spaces 74, 74 may be provided at the left and right sides, in which adjustable nozzles 75, 75 are movably fitted respectively to the left and right holding guide grooves 72, 72 while the adjustable nozzles 75, 75 are connected respectively to the medicine passages 77, 77 through the connecting pipes 76, 76.

In this case, by moving the one-side adjustable nozzle 75 relative to the other-side adjustable nozzle 75, the nozzle pitch can be suitably adjusted similarly to the third embodiment. Additionally, in this second modified example, the respective adjustable nozzles 75 approach or separate relative to each other thereby allowing the nozzle pitch to take L7 at the maximum-separated state and L8 at the minimum and approached state, so that the nozzle pitch can be adjusted within a range which is two times that in the above-mentioned third embodiment thus extending the application range.

In the first embodiment, the tapered spray hole 28, 44 has been exemplified as the spray hole. In the second embodiment, the spray hole 36 having the tapered section 36B has been exemplified as the spray hole. In the third embodiment, exemplification as the spray hole has been made on the spray hole 56, 62 which is formed straight-shaped and has axially the same diameter. However, the spray hole is not limited to these, so that it is preferable to suitably change the shape of the spray hole in accordance with the spray condition of the medicine.

In the above-mentioned third embodiment, explanation has been made on an example in which the ellipse-shaped left and right direction guide groove 58 is formed as the left and right direction guide section, in which the adjustable nozzle 61 is fitted in the left and right direction guide groove 58. However, a left and right guide projection section may be provided as the left and right direction guide section, in which the adjustable nozzle is slidably fitted to the left and right direction guide projection.

In the above-mentioned third embodiment, description has been made such that the nozzle holding projection section 59 is formed while the annular groove 61A is formed in the adjustable nozzle 61, so that the nozzle holding projection section 59 and the annular groove 61A are in engagement with each other. However, a nozzle guide may be formed as a depressed groove while the adjustable nozzle may be formed with a projection section to be engaged with the depressed groove.

In the above-mentioned respective embodiments, description has been made such that the capsule accommodating hole 12 is formed as the medicine accommodating chamber, in which the capsule K storing therein the medicine is inserted in the capsule accommodating hole 12. However, the medicine may be supplied directly into the medicine accommodating chamber from the outside by using a separate supplying tool or the like. In this case, the capsule is not to be required.

INDUSTRIAL USABILITY

As discussed above, the medicine administering device for nasal cavities, according to the present invention and a method of using the same can be applied to ones by which fine powder, granule or the like filled in a capsule can be sucked upon breaking the capsule.

Claims

1. A medicine administering device for nasal cavities, characterized by being arranged such that a separation-distance between left and right nozzles in left and right directions is adjustable in conformity with a distance between left and right nasal cavities of a patient when powder-like medicine within a medicine accommodating chamber is sprayed from the left and right nozzles respectively into the left and right nasal cavities of the patient under a condition where the powder-like medicine has been accommodated in the medicine accommodating chamber.

2. A medicine administering device for nasal cavities, characterized by comprising a medicine accommodating chamber accommodating therein powder-like medicine, air supply means for supplying air toward the medicine accommodating chamber, passage means including left and right medicine passages through which the medicine in the medicine accommodating chamber is supplied toward left and right nasal cavities of a patient by air supplied from the air supply means, and distance-adjustable nozzle means disposed at ejection side of the medicine passage of the passage means and adjustable in conformity with a distance between the nasal cavities of the patient in order to spray the medicine under a condition to be inserted into the left and right nasal cavities of the patient.

3. A medicine administering device for nasal cavities, characterized by comprising a medicine accommodating chamber accommodating therein powder-like medicine, air supply means for supplying air toward the medicine accommodating chamber, passage means including left and right medicine passages through which the medicine in the medicine accommodating chamber is supplied toward left and right nasal cavities of a patient by air supplied from the air supply means, and distance-adjustable nozzle means including left and right nozzles disposed respectively at ejection sides of medicine passages of said passage means in order to spray the medicine under a state to be inserted respectively in the left and right nasal cavities of the patient, wherein at least one nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is disposed rotatable, and said nozzle is disposed at a position eccentric to a rotational center.

4. A medicine administering device for nasal cavities, as claimed in Claim 3, characterized in that the at least one nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is disposed detachable to said passage means.

5. A medicine administering device for nasal cavities, as claimed in Claim 3, characterized in that a spray hole of the nozzle constituting said distance-adjustable nozzle means is formed generally straight.

6. A medicine administering device for nasal cavities, as claimed in claim 4, characterized in that a spray hole of the nozzle constituting said distance-adjustable nozzle means is formed generally straight.

7. A medicine administering device for nasal cavities, as claimed in Claim 3, characterized in that a spray hole of the nozzle constituting said distance-adjustable nozzle means is formed eccentric.

8. A medicine administering device for nasal cavities, as claimed in Claim 4, characterized in that a spray hole of the nozzle constituting said distance-adjustable nozzle means is formed eccentric.

9. A medicine administering device for nasal cavities, characterized by comprising a medicine accommodating chamber accommodating therein powder-like medicine, air supply means for supplying air toward the medicine accommodating chamber, passage means including left and right medicine passages through which the medicine in the medicine accommodating chamber is supplied toward left and right nasal cavities of a patient by air supplied from the air supply means, and distance-adjustable nozzle means including left and right nozzles disposed respectively at ejection sides of medicine passages of said passage means in order to spray the medicine under a state to be inserted respectively in the left and right nasal cavities of the patient, wherein at least one nozzle of the left and right nozzles constituting the distance-adjustable nozzle means is disposed movable in left and right directions relative to the other nozzle.

10. A medicine administering device for nasal cavities, as claimed in Claim 9, characterized in that said distance-adjustable nozzle means includes a left and right direction guide section for guiding the at least one nozzle of the left and right nozzles, and a nozzle holding section for holding the nozzle when the nozzle is moved by the left and right direction guide section.

11. A medicine administering device for nasal cavities, as claimed in Claim 9, characterized in that the adjustable nozzle of the left and right nozzles constituting said distance-adjustable nozzle means and the passage means are connected by a connecting pipe having a flexibility.

12. A medicine administering device for nasal cavities, as claimed in Claim 10, characterized in that the adjustable nozzle of the left and right nozzles constituting said distance-adjustable nozzle means

and the passage means are connected by a connecting pip having a flexibility.

13. A medicine administering device for nasal cavities, as claimed in Claim 1, characterized in that the medicine is supplied into said medicine accommodating chamber by a capsule or a separate supplying tool.

14. A medicine administering device for nasal cavities, as claimed in Claim 2, characterized in that the medicine is supplied into said medicine accommodating chamber by a capsule or a separate supplying tool.

15. A medicine administering device for nasal cavities, as claimed in Claim 3, characterized in that the medicine is supplied into said medicine accommodating chamber by a capsule or a separate supplying tool.

16. A medicine administering device for nasal cavities, as claimed in Claim 9, characterized in that the medicine is supplied into said medicine accommodating chamber by a capsule or a separate supplying tool.

17. A medicine administering device for nasal cavities, as claimed in Claim 2, characterized in that said air supply means includes means for supplying air by a pump.

18. A medicine administering device for nasal cavities, as claimed in Claim 3, characterized in that said air supply means includes means for supplying air by a pump.

19. A medicine administering device for nasal cavities, as claimed in Claim 9, characterized in that said air supply means includes means for supplying air by a pump.

20. A method of using a medicine administering device for nasal cavities, characterized by adjusting a separation-distance of left and right nozzles in left and right directions in conformity with a distance between nasal cavities of a patient by rotating at least one nozzle of the said nozzles so as to cause the nozzle to be eccentric to the other nozzle or by making a slide-movement of at least one nozzle of the left and right nozzles in the left and right directions relative to the other nozzle, when powder-like medicine within a medicine accommodating chamber is sprayed from the left and right nozzles respectively into the left and right nasal cavities of the patient under a condition where the powder-like medicine has been accommodated in the medicine accommodating chamber.

FIG.1

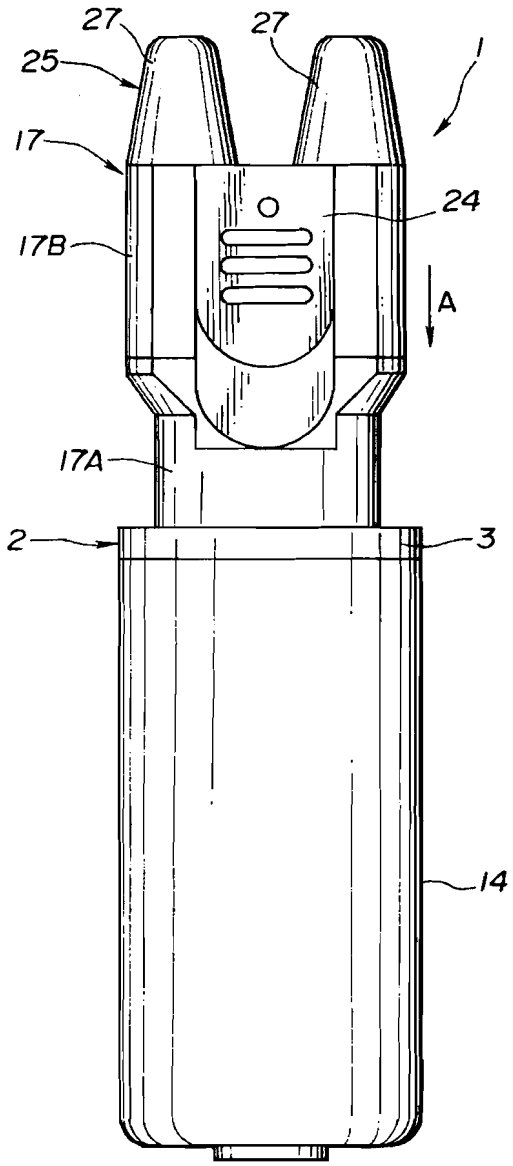
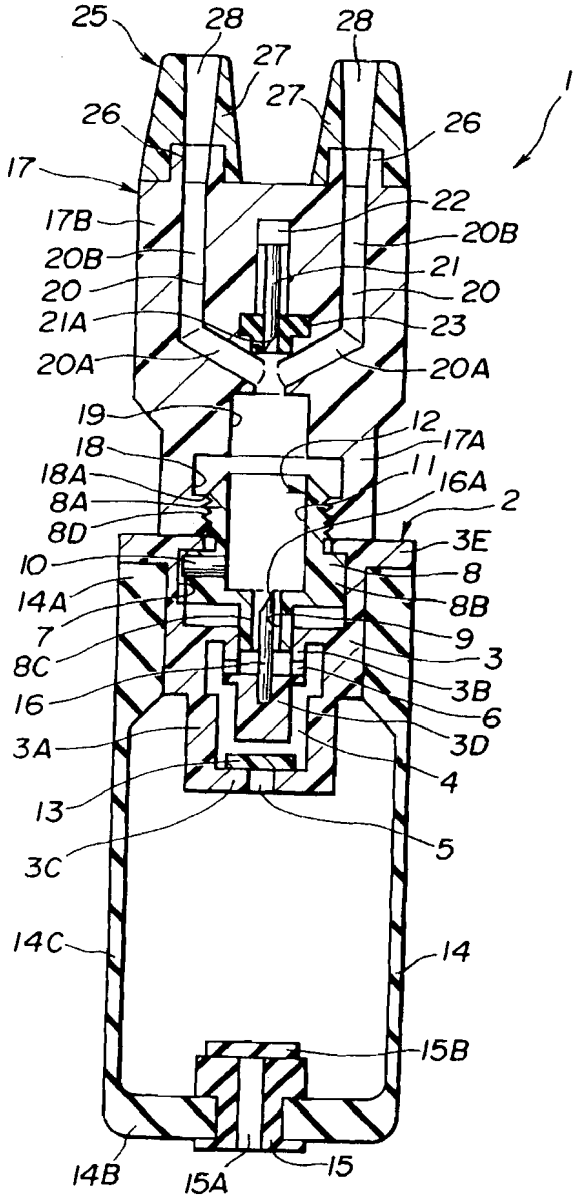


FIG.2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11
16A
8A
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8D
3E
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8
14A
8B
7
9
8C
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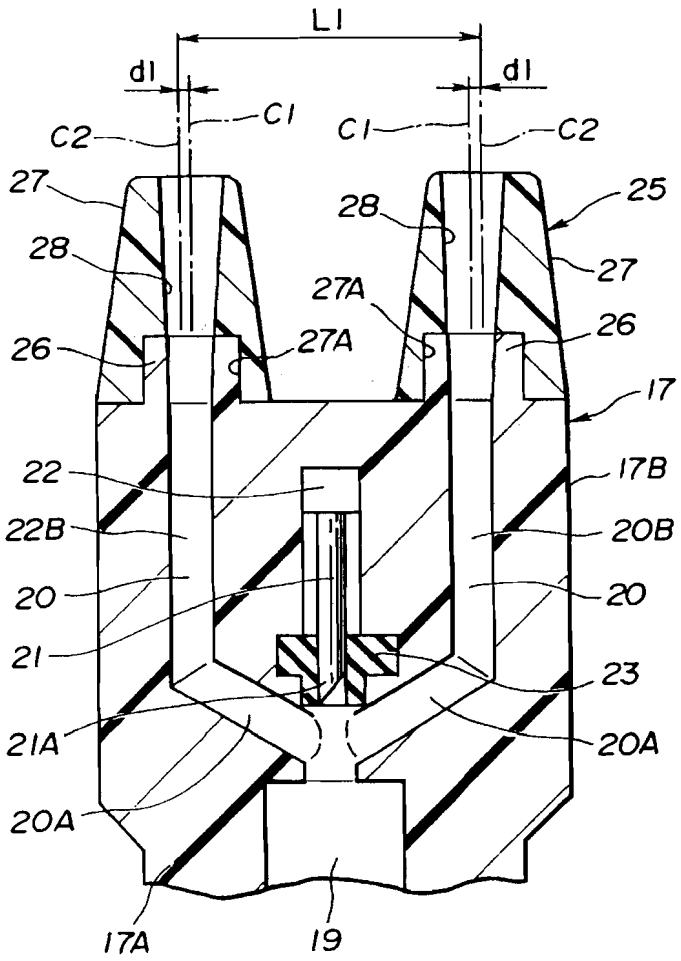
FIG.3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17A
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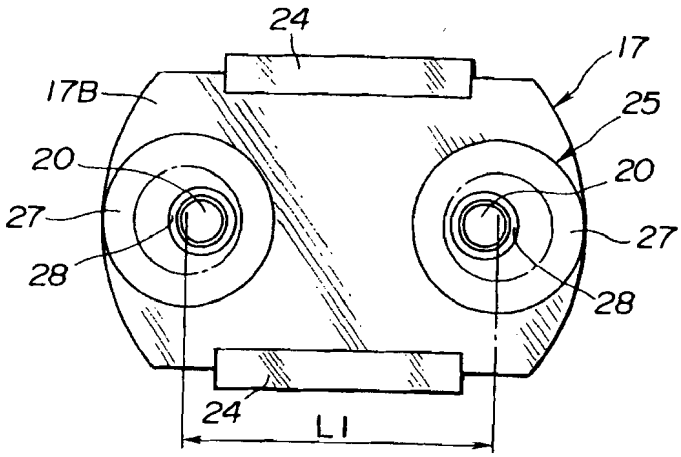
FIG.4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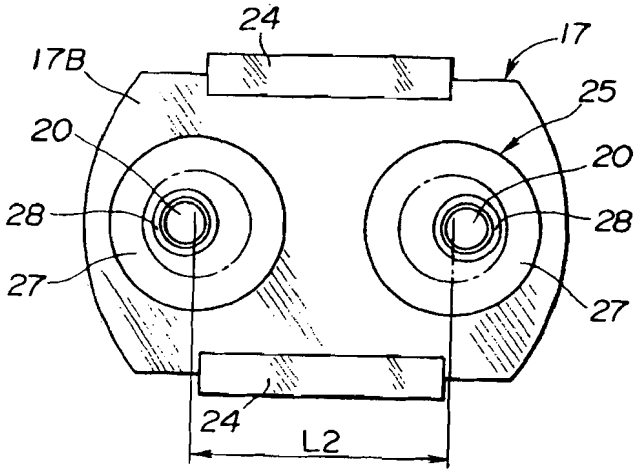
L1

FIG.6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L2

FIG.5

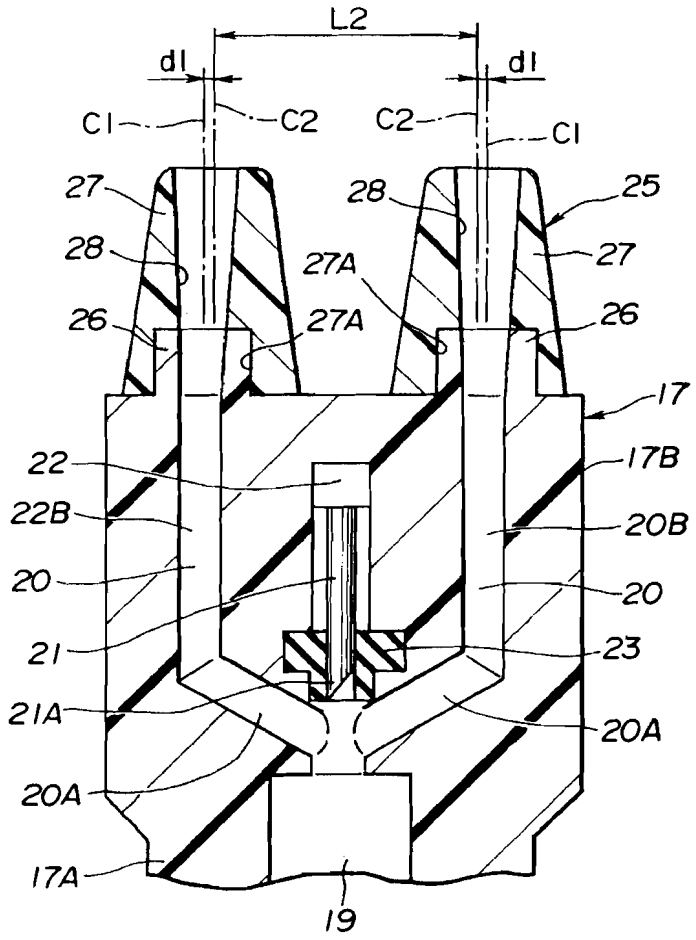
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FIG.7

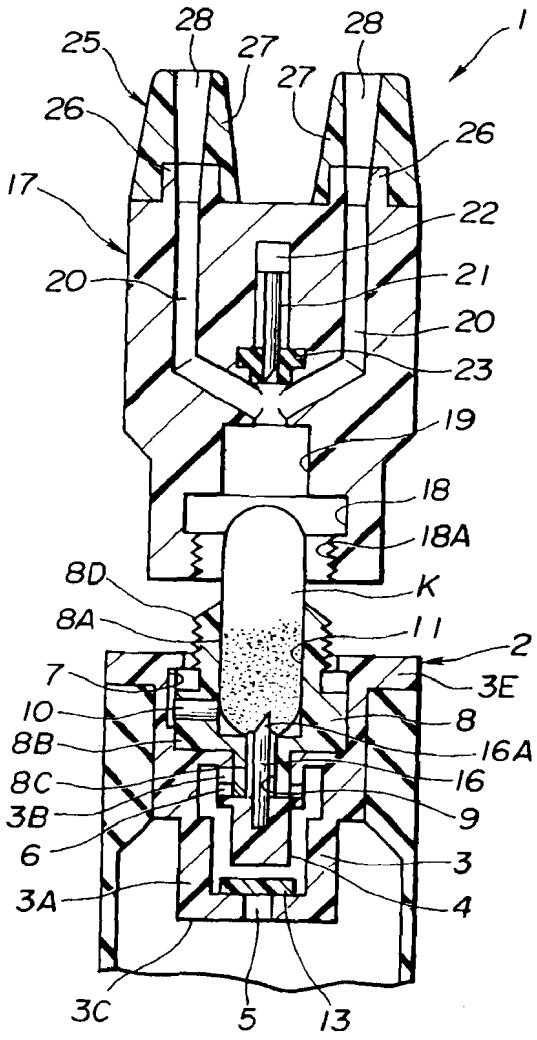
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FIG.8

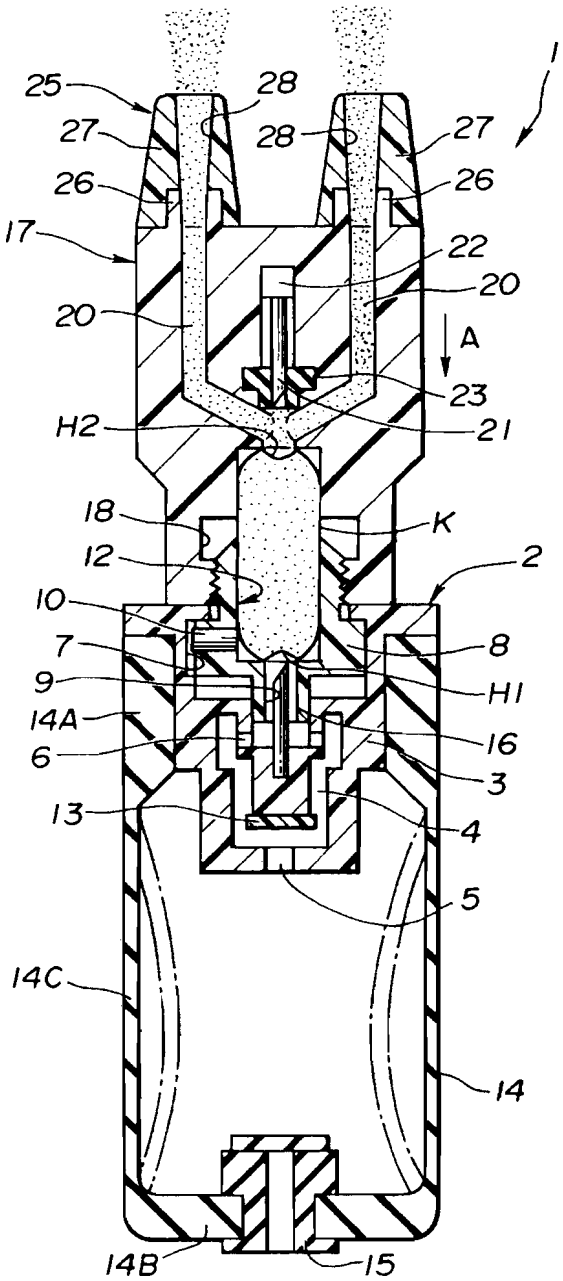
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FIG.9

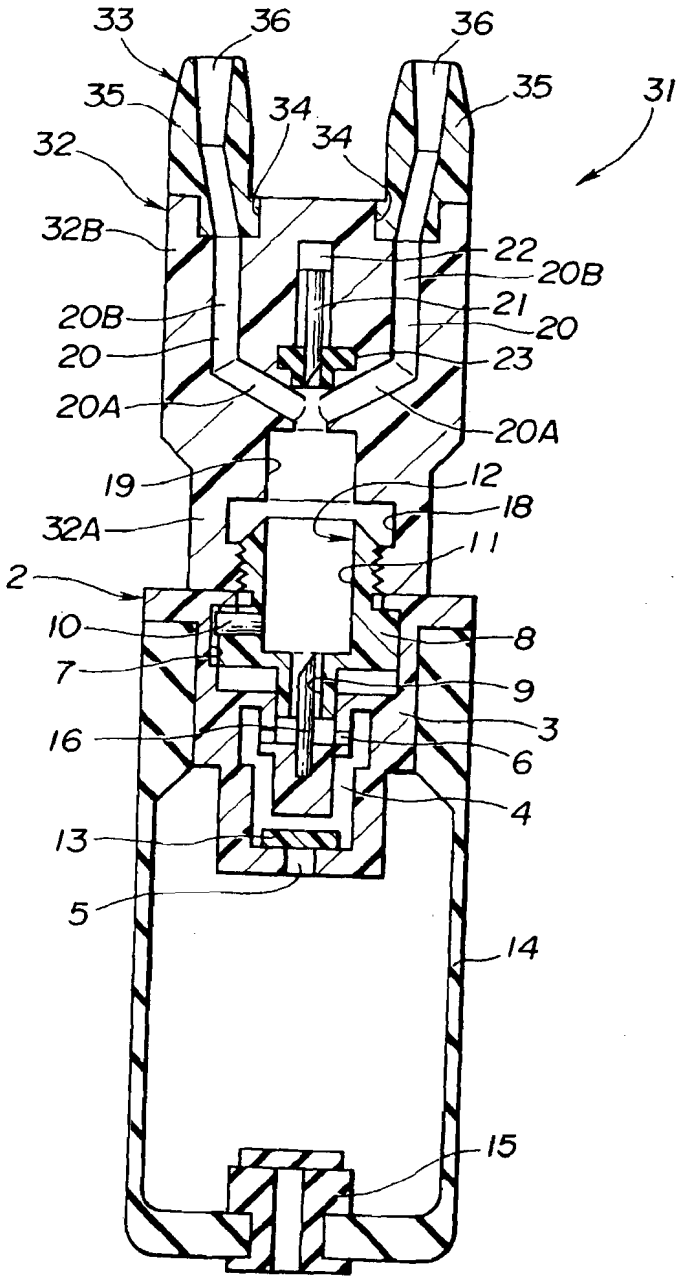
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FIG.10

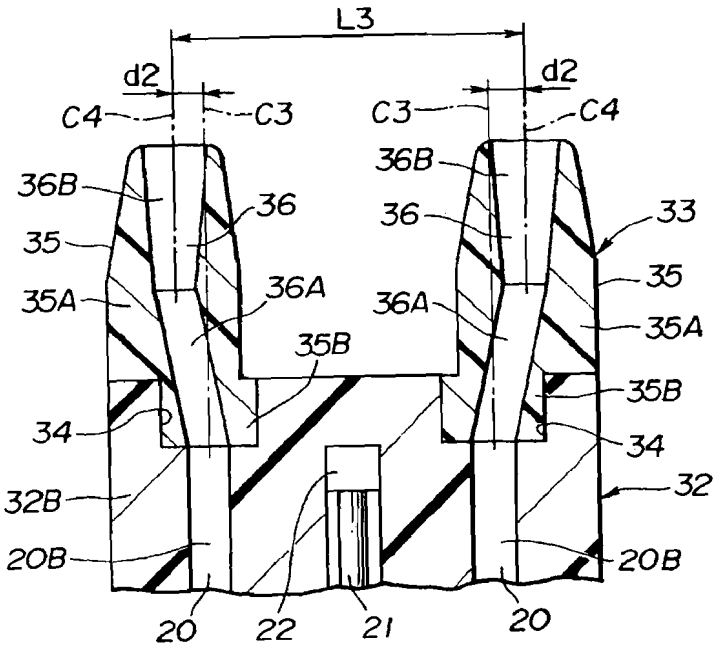
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FIG.11

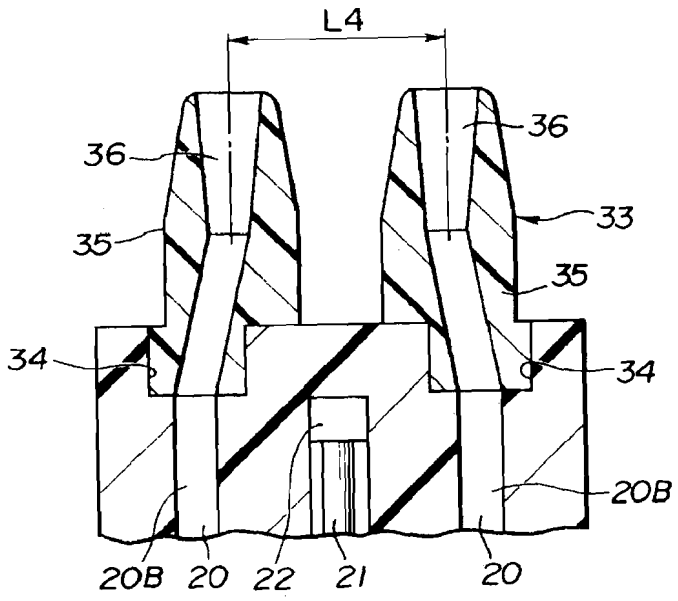
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FIG.12

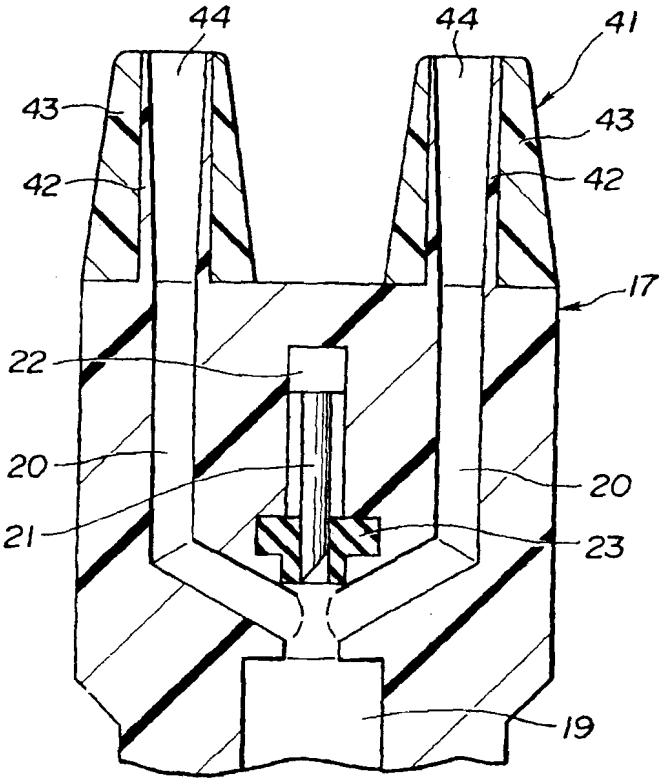
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FIG.13

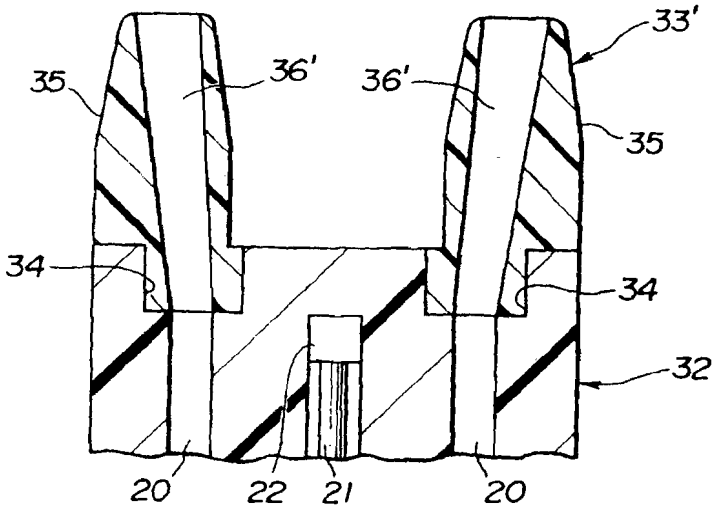
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FIG.14

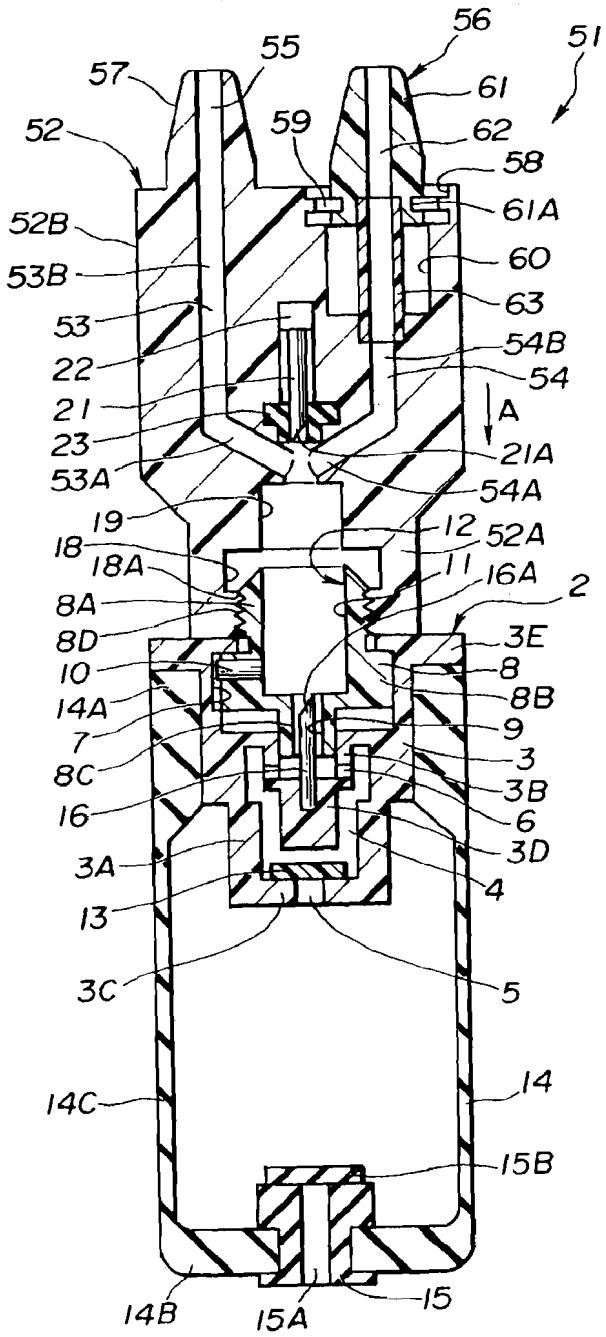
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FIG.15

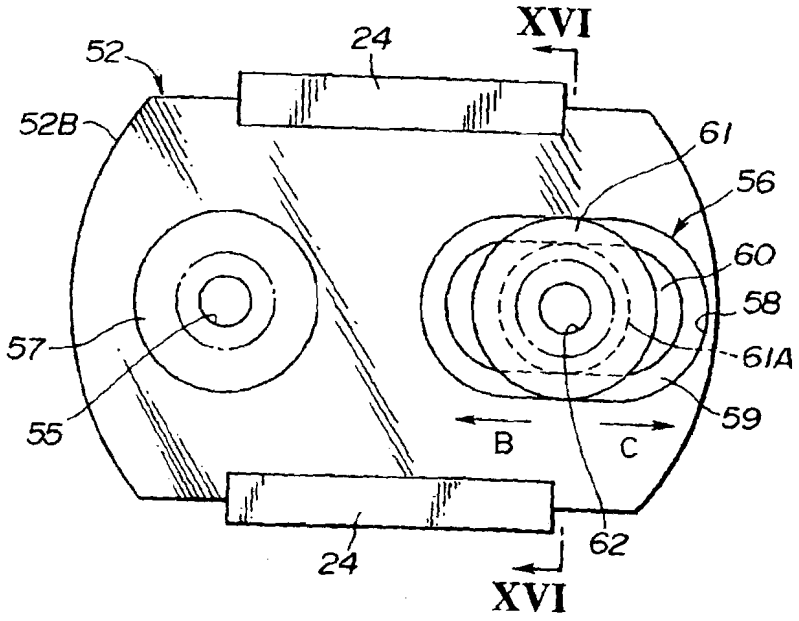
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FIG.16

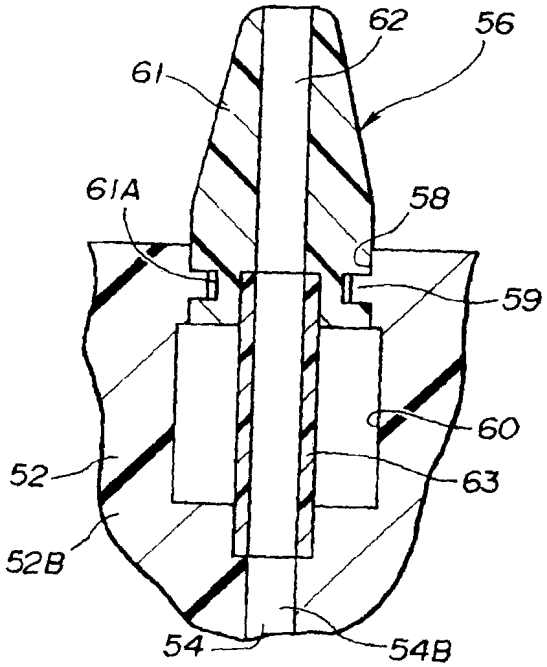
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FIG.17

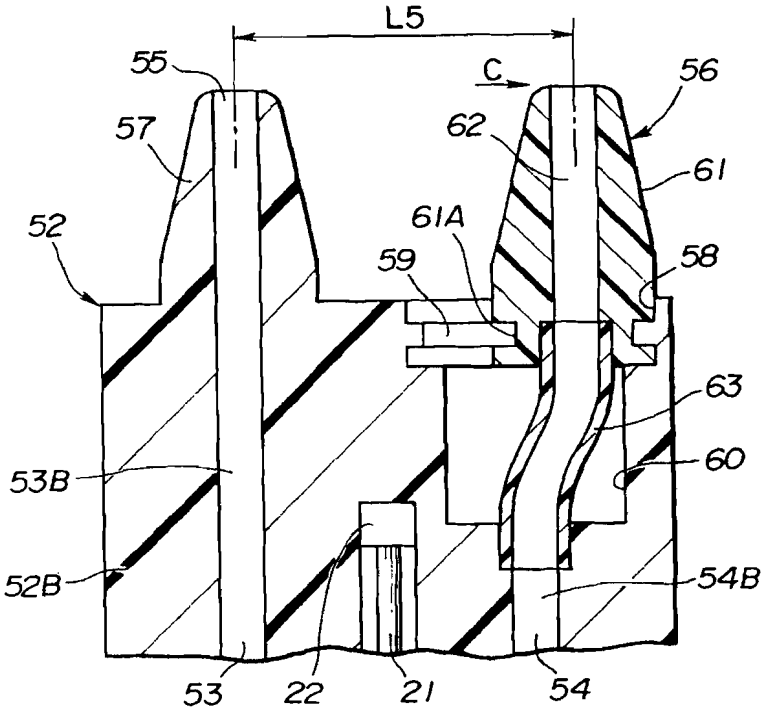
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FIG.18

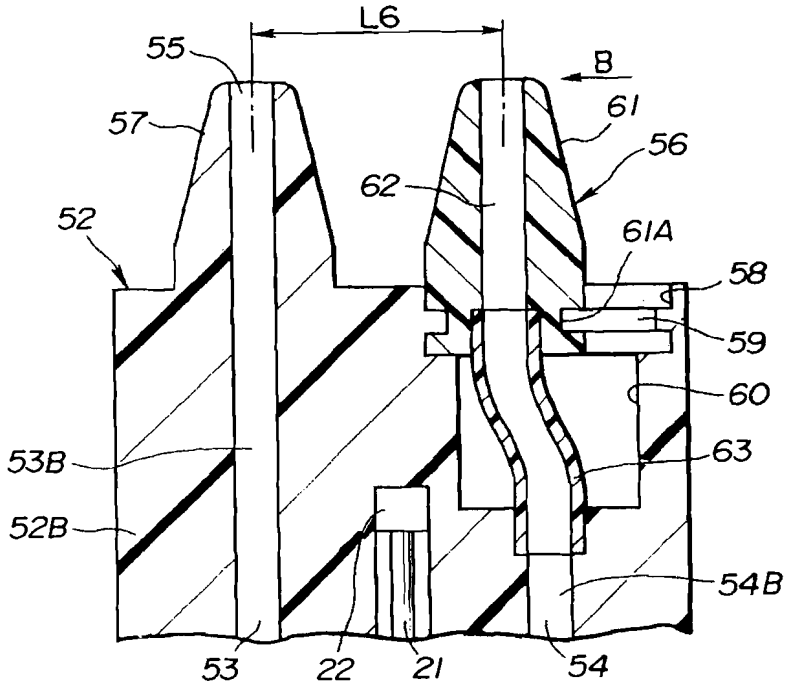
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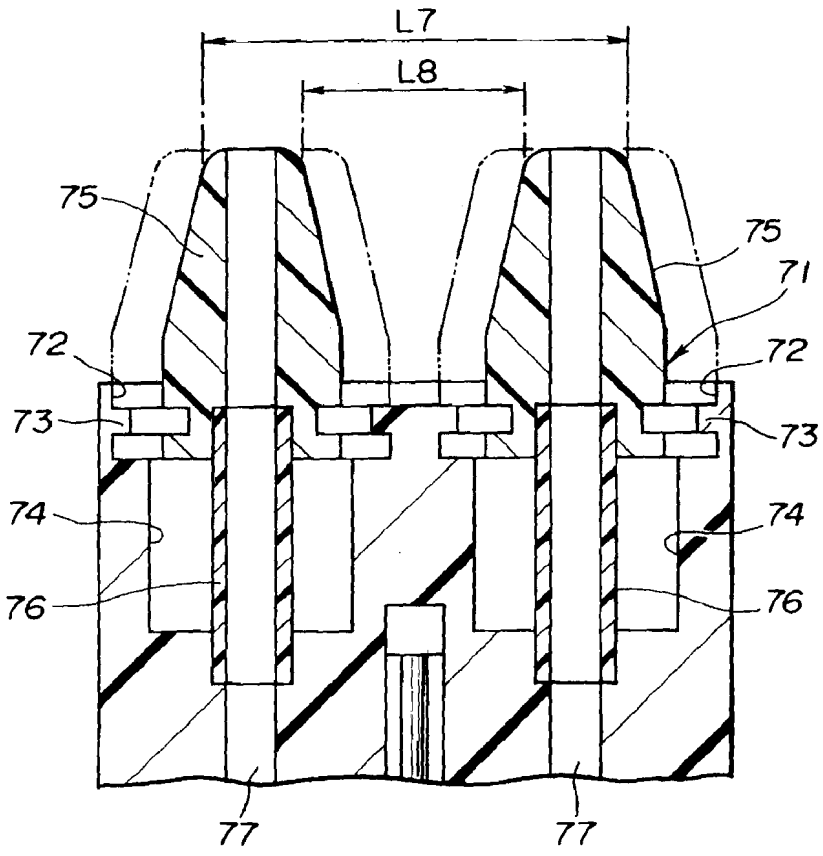
FIG.19



INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/01798

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl^6 A61M15/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int. Cl^6 A61M15/08

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1926 - 1996
Kokai Jitsuyo Shinan Koho	1971 - 1996
Toroku Jitsuyo Shinan Koho	1994 - 1996

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	JP, 3003998, U (Koei Kawakami), November 1, 1994 (01. 11. 94)(Family: none)	1 2 - 20
A	JP, 6-142157, A (Shinko Kagaku K.K.), May 24, 1994 (24. 05. 94)(Family: none)	1 - 20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
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"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
October 2, 1996 (02. 10. 96)	October 8, 1996 (08. 10. 96)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)